Neurocognitive Mechanisms of Learning and Decision-Making in Adolescent-OCD: A Computational Approach

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Declaration

I hereby declare that this thesis is the result of my own work and includes nothing which is the outcome of work done in collaboration except as declared in the preface and specified in the text, and that it is not substantially the same as any work that has already been submitted before for any degree or other qualification except as declared in the preface and specified in the text. This dissertation does not exceed the prescribed word limit for the Degree Committee for the Faculty of Biology.

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Abstract

Early-onset obsessive-compulsive disorder (OCD) is substantially less researched than adult-OCD, resulting in prevalent equivocation surrounding the neurocognitive profile of child-OCD. Research into this area is pivotal as population studies report that youths with OCD struggle significantly in academic settings. In the General Introduction of this thesis, I reviewed existing literature and found that strikingly, young patients do not show impairment on features that are considered both hallmarks of adult OCD and tightly linked to disorder symptomatology, such as response inhibition and cognitive flexibility. Among the characteristics that are thought to be present in children and adolescents with OCD are abnormal decision-making under uncertainty and impaired learning, and I decided to focus on these features as they may be driving poor academic attainment in young people with the disorder. In addition, I sought to investigate other cognitive processes that have not been well-researched in adolescent-OCD but are found to be robustly altered in adult OCD such as goal-directed/model-based reasoning, meta-cognition, and feedback sensitivity. I aimed to delineate these various processes using a battery of suitably complex cognitive tasks. Moreover, I highlighted that majority of past studies fail to find differences between young patients and controls due to behavioural signatures being too subtle to be uncovered by standard statistical analyses. Hence, I employed computational modelling of cognitive task data to disentangle latent decision-making processes displayed by adolescents with OCD.

In Chapter 2, I modelled data from the Wisconsin Card Sorting task, a frequently used paradigm of cognitive flexibility, and confirmed that youths with OCD show equivalent performance on the task to controls. Only patients on serotonergic medication showed increased response latencies and a tendency to make unique errors (choosing a deck associated with no rule present on the test card). Next, in Chapter 3, I sought to understand instrumental and Pavlovian learning, and whether adolescents with OCD show increased punishment sensitivity on a novel aversive Pavlovian-to-Instrumental Transfer paradigm. Once again, patient performance was equivalent to that of controls. Hence, the remaining chapters were dedicated to probing behaviour on probabilistic paradigms. In Chapter 4, I formally investigated model-based and model-free learning using a well-validated two-step decision-making task, and fit a reinforcement learning drift diffusion model to both choice and reaction time data. Patients showed increased exploration on the task as well as faster and more erratic decisions compared to controls. Nonetheless, model-based learning was equivalent between groups. In the penultimate chapter, I demonstrate on a predictive-inference task that patients with OCD update their choices more frequently compared to controls independent of prediction error magnitude. Finally, in Chapter 6, I administered a probabilistic reversal learning paradigm to a large

sample of 50 adolescent patients and 53 matched controls. Standard analyses revealed a significant reversal learning deficit in patients with OCD, wherein they displayed more errors and a lower propensity to repeat choices following positive feedback during the post-reversal phase. Crucially, computational modelling revealed striking group differences where adolescents with OCD displayed elevated reward learning and lower punishment learning, increased exploration, and decreased perseveration compared to controls. In the General Discussion, I emphasise that atypical learning and decision-making in adolescent-OCD are more pronounced on probabilistic tasks, where task environments are more volatile. Results are partly discussed in the context of the uncertainty model of OCD, where subjective feelings of doubt experienced by patients drive compulsive behaviours such as checking and certainty-seeking in daily life, alongside excessive exploration on probabilistic tasks. I also consider various explanations for cognitive distinctions between adult- and adolescent-OCD. More general implications of the findings are discussed for understanding OCD in the context of adolescent development and for treatment/support strategies.

Contents

Chapter 1: General Introduction

1.1 Clinical and epidemiological characteristics of paediatric OCD

Obsessive-compulsive disorder (OCD) is a highly disabling psychiatric disorder affecting roughly 2-3% of children, adolescents, and adults worldwide (Kalra & Swedo, 2009; Karno, Golding, Sorenson, & Burnam, 1988; Ruscio, Stein, Chiu, & Kessler, 2010). Many cases of OCD seen in adults begin in childhood, as age of disorder onset follows a bimodal trend, peaking at approximately 10 years of age and again in early adulthood (Geller, 2006; Geller et al., 1998). Furthermore, within a large ethnically diverse sample of adult patients (N = 3711), the mean age of OCD onset was in late adolescence (17.9 years) (Brakoulias et al., 2017). Indeed, experiences during childhood play a significant role in the development of OCD. Research has demonstrated that neurodevelopmental, behavioural, personality, environmental risk factors in childhood were strong predictors of receiving a diagnosis of OCD or experiencing obsessive-compulsive symptoms in adulthood (Grisham et al., 2011). In addition, healthy children who report obsessive and compulsive behaviours are significantly more likely to meet diagnostic criteria for OCD in adulthood, compared to children without such traits (Fullana et al., 2009). Surprisingly, however, there is also contrasting research highlighting a lack of diagnostic continuity between OCD in childhood and in adulthood. A meta-analysis exploring data from 16 study samples (N=521) found that the mean persistence rate for full-OCD (severe enough to meet diagnostic criteria) from childhood to adulthood was only 41% (Stewart et al., 2004). Additionally, only one-third to one-half of adults with OCD report childhood-onset (Rasmussen & Eisen, 1992), although such self-report data may not be very reliable.

OCD as a whole is characterised by recurring unwanted thoughts, ideas and sensations (obsessions), as well as repetitive ritualised actions or thoughts that a person feels compelled to perform (compulsions) (American Psychiatric Association, 2013). These general characteristics apply to both adults and children with the disorder and indeed the Diagnostic and Statistical Manual-5 (DSM-5) outlines the same diagnostic criteria for both child and adult OCD. However, research has uncovered critical differences between the age-groups. Among them, adult-onset OCD occurs more prominently in women (Karno et al., 1988; Noshirvani, Kasvikis, Marks, Tsakiris, & Monteiro, 1991), while early-onset OCD is associated with a male preponderance (Deepthi, Sagar Kommu, Smitha, & Reddy, 2018; Geller et al., 2001; Mancebo et al., 2008; Taylor, 2011). Moreover, research reports the heritability of OCD is greater in paediatric patients compared to adult patients (Van

Grootheest, Cath, Beekman, & Boomsma, 2005) suggesting that early-onset OCD may be a developmental subtype of the disorder.

While both paediatric and adult patients typically display compulsions related to checking, ordering, cleaning, and washing (Thomsen et al., 2000) (Leckman et al., 1997; Stewart et al., 2007), paediatric patients report decreased mental rituals compared to adults with the disorder (Mancebo et al., 2008). Moreover, the content of paediatric obsessions is distinct from adult obsessions, as child patients report higher rates of aggressive and miscellaneous intrusions (Geller et al., 2001; Mancebo et al., 2008). Additionally, affected children tend to have fewer and more manageable obsessions than affected adults (Farrell & Barrett, 2006), and 40% of children deny that obsessions drive their compulsive acts (Swedo, Rapoport, Leonard, Lenane, & Cheslow, 1989). This could be evidence for compulsions developing prior to obsessions in children with the disorder. Alternatively, children with OCD may not yet be able to verbalise their obsessions, leading to clinicians underestimating their frequency of obsessions.

A majority of patients with OCD will present with a comorbid disorder in their lifetime (Rasmussen & Eisen, 1992). The most common comorbid conditions in adults with OCD include anxiety disorders, mood disorders, impulse control disorders, substance use disorders, and phobias (Ruscio, Stein, Chiu, & Kessler, 2010; Brakoulias, Starcevic, & Belloch, 2017). Children with OCD present different patterns of comorbid diagnoses, with higher likelihood of developing comorbid tic disorder, attention deficit hyperactivity disorder (ADHD), and developmental disabilities (Kalra & Swedo, 2009; Leonard et al., 2001; Taylor et al., 2011). Additionally, the most common personality disorder associated with paediatric OCD was found to be avoidant personality disorder while obsessive-compulsive personality disorder was more prevalent in adult OCD patients (Thomsen & Mikkelsen, 1993).

There are also reported differences in clinical presentation between older and younger children with OCD. Namely, those with very early-onset (below 10 years) showed higher rates of comorbid tics, more frequent ordering and repeating compulsions, and greater parent-reported psychosocial difficulties (Nakatani et al., 2011). In another study, adolescents with OCD reported more religious obsessions than younger patients, while younger patients showed lower insight compared to adolescents, and displayed more comorbid disruptive disorders and separation anxiety (Geller et al., 2001). This is intriguing as it demonstrates that clinical presentation of OCD changes with age in childhood.

Despite being clinically divergent, treatments for paediatric- and adult-OCD are identical. OCD symptoms in adults and children improve following the administration of high doses of selective serotonin reuptake inhibitors (SSRIs) (Abramowitz, Whiteside, & Deacon, 2005; Bloch, McGuire, Landeros-Weisenberger, Leckman, & Pittenger, 2010), and cognitive behavioural therapy (CBT) including exposure response prevention (ERP) (Abramowitz et al., 2005; Skapinakis et al., 2016; Whittal, Thordarson, & McLean, 2005). However, there appears to be differences in treatment efficacy, as OCD remission rate amongst youths is reported to be higher than in adults (Mancebo et al., 2014). Juveniles with OCD are also more likely to receive medication treatment at a younger age than adults with early onset OCD (Mancebo et al., 2008), suggesting that detection and treatment of the disorder in childhood could be linked to higher chances of recovery.

Living with OCD during the key developmental periods of childhood and adolescence can greatly impact a young person's daily functioning, and it is unsurprising that children with OCD typically have a lower quality of life compared to healthy children (Weidle, Ivarsson, Thomsen, Lydersen, & Jozefiak, 2015). Adding to this, academic attainment is reported to be impeded as a result of the disorder. Many school-going children with OCD report difficulty concentrating on schoolwork and completing assignments (Piacentini, Bergman, Keller, & McCracken, 2003), and a more recent study found that child patients show significantly poorer mathematics ability compared to healthy children (Negreiros, Belschner, Selles, Lin, & Stewart, 2018). In addition, a nationwide cohort study based in Sweden that investigated education milestones in over 2 million participants reported that subjects diagnosed with OCD (15120 subjects) in childhood were less likely to finish secondary school and pursue postgraduate education (Pérez-Vigil et al., 2018). These trends are highly concerning and it is crucial that present research is devoted to determining the cognitive characteristics of childhood-OCD to better understand why affected children are struggling academically. One such study has recently found that adolescent patients show marked learning impairments (Gottwald et al., 2018), but hitherto it is uncertain why children with OCD display these specific neuropsychological deficits which actually differ to an extent from typical cognitive findings in adults with OCD (see next section). It is crucial to understand the mechanisms underlying these deficits to guide the design of suitable interventions that could aid children with OCD who are struggling academically.

1.2 Cognitive characteristics of paediatric OCD

Among the key areas of research into cognition in OCD are cognitive flexibility, reversal learning, response inhibition, decision-making, planning, action monitoring, and the imbalance between goal-

directed and habit-directed control. Most of these domains have been labelled potential endophenotypes of OCD which means they are heritable quantitative traits associated with increased genetic risk for the disorder (Gottesman & Gould, 2003). This is because deficits in these domains also occur in the unaffected first-degree relatives (UFDRs) of adult OCD patients at a higher rate than the general population (Chamberlain & Menzies, 2009). Despite this, as will become increasingly apparent in this section, deficits in several domains are not as prominent in young people with the disorder, implying a cognitive divergence between child- and adult-OCD.

1.2.1 Cognitive Flexibility

Cognitive flexibility is defined as the ability to adapt one's attention to different tasks, strategies and stimuli which are relevant, while simultaneously disengaging from/ignoring irrelevant stimuli. Researchers have studied this function using set-shifting paradigms, such as the Wisconsin Card Sorting Task (WCST) (Grant & Berg, 1948) and the CANTAB Intra-Extra Dimensional Set Shift Task (ID/ED) (Downes et al., 1989), as well as using other executive switching tasks such as the Trail-Making Task B (TMT-B) (Reitan & Wolfson, 1985), and task switching tests. There are key differences between set-shifting paradigms and the latter two tasks: set-shifting involves shifting attention between different cognitive sets by learning from *feedback* to follow a certain rule, while the other switching tasks do not involve feedback learning and instead require shifting attention after being *cued* to switch.

The WCST involves sorting cards based on a specific rule that can change from time to time (e.g. from colour to shape). Findings on the WCST are mixed in paediatric populations, as on the one hand, children with OCD have been reported to be more perseverative, commit more overall errors, and complete fewer categories on the WCST compared to healthy controls (Baykal et al., 2014; Isik Taner, Erdogan Bakar, & Oner, 2011; M. S. Shin et al., 2008). This indicates that children with OCD are less able to direct attention to task-relevant information. In addition, Andrés et al. (2007) found that paediatric patients also make more non-perseverative errors also suggesting an impairment with attention and learning in general. Nonetheless, majority of studies report that children with OCD show no impairments on the WCST (Beers et al., 1999; Geller et al., 2018; Gruner et al., 2012; Kodaira et al., 2012; Ornstein, Arnold, Manassis, Mendlowitz, & Schachar, 2010). In contrast, adults with OCD typically commit more perseverative errors on the WCST compared to age-matched controls (Aigner et al., 2007; Bucci et al., 2007; Cavedini, Zorzi, Piccinni, Cavallini, & Bellodi, 2010; Lucey et al., 1997; Okasha et al., 2000; Paast, Khosravi, Memari, Shayestehfar, & Arbabi, 2016; Tükel et al., 2012). Gruner et al. (2012) suggest that WCST-impairments may be dependent on medication, as authors reported that paediatric OCD patients treated with SSRIs completed fewer

categories on the WCST while medication-naïve patients showed no impairment. Yet, Andrés et al. (2007) also checked for effects of medication but did not find any differences between medicated and unmedicated child patients on the task.

The ID/ED task dissociates the effects of intra-dimensional (ID) and extra-dimensional (ED) shifts which are implicit in the WCST (Rogers, Andrews, Grasby, Brooks, & Robbins, 2000). ID shifts involve the formation of an attentional set towards a stimulus dimension (e.g. lines), and then 'shifting' between test stimuli within the same dimension. ED shifts involve attending to a new stimulus dimension (e.g. shapes) that was previously irrelevant. Adults with OCD more often than not show increased ED errors on the task (Chamberlain, Fineberg, Menzies, et al., 2007; Chamberlain, Müller, et al., 2006; Vaghi, Vértes, et al., 2017; Watkins et al., 2005) (see Chamberlain et al., manuscript submitted for meta-analysis), suggesting that they are perseverating at responding to the dimension that is no longer relevant. In contrast, Gottwald et al. (2018) discovered that adolescents with OCD made more errors compared to controls in the pre-ED shift portion of the task, which includes discrimination and reversal learning (ID shifts), but not attentional set shifting (ED shifts). However, Kim et al. (2018) reported that children with generalised anxiety disorder (GAD), and not OCD, showed poor learning in the pre-ED phase. However, this effect disappeared after the authors statistically controlled for medication status suggesting an interaction between anxiety and medication on attentional learning. Different age ranges could also account for these differences as Kim et al. recruited children as young as 7 years old in their study, while Gottwald et al. only studied adolescents. Hybel et al. (2017) also did not find differences in cognitive flexibility (measured via post-ED errors) on the ID/ED task between child OCD patients and controls but they did not report pre-ED scores in their analysis.

Next, the TMT-B requires participants to alternate drawing lines between letters and numbers (e.g 1-A-2-B). One study reported children with OCD made slower movements on the test compared to controls (Ornstein et al., 2010), which has also been demonstrated in adults with OCD (Ozcan, Ozer, & Yagcioglu, 2016). However, most other studies employing the test do not find any significant deficits in children with OCD (Beers et al., 1999; Garcia-Delgar et al., 2018), and even studies that found OCD-related impairments on the WCST reported no significant performance deficits on the TMT-B (Andrés et al., 2007; Shin et al., 2008). This indicates that the WCST may be more sensitive to set-shifting deficits in OCD compared to the TMT-B. Nevertheless, Gruner et al. (2012), using diffusion tensor imaging, uncovered brain white matter abnormalities in children with OCD pertaining to their task performance. Higher fractional anisotrophy (more diffusion of water molecules along a tract, reflecting better white matter connectivity) in the cingulum bundle, including

the anterior cingulate cortex (ACC), was correlated with better performance on the TMT-B within only the patient group. It was inferred that this atypical diffusion serves as a compensatory mechanism, allowing young patients to perform similarly to their healthy counterparts (Gruner et al., 2012).

Task switching tests are similar in implementation to the TMT-B, as they involve switching from attending to one feature of a stimulus (e.g. shape) to another (e.g. colour) when cued. Studies generally revealed no behavioural differences between paediatric patients and controls on such tasks (Britton et al., 2010; Woolley et al., 2008). However, Wolff et al. (2017) demonstrated that OCD patients had slower reaction times on memory-based switching (requires remembering when to switch tasks, e.g. switching between attending between 'number' and 'shape' every 15 trials) but normal reaction times during cue-based switching (switching attention when provided with a cue), suggesting patients' cognitive flexibility is impacted by working memory load. Interestingly, in a separate study, adolescent patients were shown to be faster than controls at attending to previously abandoned mental sets during task switching (Wolff, Giller, Buse, Roessner, & Beste, 2018), suggesting that young OCD patients are impaired at processing new information, but are able to flexibly reactivate old mental sets. Child patients showed underactivity in rostral brain regions, specifically the inferior frontal gyrus (Britton et al., 2010) and the inferior prefrontal cortices (Woolley et al., 2008) during task switching, which mirrors findings from adult OCD (Gu et al., 2008; Vaghi, Vértes, et al., 2017). Furthermore, child OCD patients showed lower P1 event-related potential (ERP) amplitudes, as measured using EEG, during memory-based switching which corresponded to decreased activation in the right inferior frontal and temporal gyri (Wolff, Buse, Tost, Roessner, & Beste, 2017).

Summary

Evidence from the WCST suggests that children with OCD may present cognitive inflexibility but they appear to be unimpaired on other tasks in this domain. One study has suggested that adolescent patients have more of a basic learning impairment instead of a cognitive flexibility deficit (Gottwald et al., 2018) but these findings so far have not been replicated. In spite of mixed behavioural results, studies employing neuroimaging reveal crucial prefrontal-cortical brain region differences between child patients and controls during task switching tests, mirroring results from adult patients.

1.2.2 Reversal learning

Reversal learning tasks have typically been employed to study cognitive flexibility, and are also useful in probing instrumental learning and feedback processing. There are two types of reversal learning paradigms, namely deterministic and probabilistic reversal learning. During deterministic reversal learning subjects are trained to discriminate between two visual stimuli or spatial locations, one of which is rewarded every time it is chosen while the other is either unrewarded or punished. After some trials or after a learning criterion has been achieved, the outcomes associated with the stimuli are reversed. Probabilistic reversal learning is similar except outcomes associated with each stimulus are probabilistic, hence subjects must learn to respond to the stimulus that delivers positive feedback most of the time (e.g. 80% of the time) over a different stimulus that delivers positive feedback only a small proportion of the time (e.g. 20% of the time). Probabilistic reversal learning tasks differ considerably from others studying this domain as the feedback provided is not always reliable, adding an extra layer of complexity and enables investigation of learning under uncertainty.

Classically, adults with OCD are observed to be unimpaired on both deterministic and probabilistic reversal learning tasks compared with healthy controls (Chamberlain, Fineberg, Blackwell, et al., 2007; Ersche et al., 2011; Remijnse et al., 2009; Remijnse et al., 2006; Valerius, Lumpp, Kuelz, Freyer, & Voderholzer, 2008) although they have been found to show abnormally reduced right medial and lateral orbitofrontal cortex (OFC) activity when completing deterministic and probabilistic versions of the task (Chamberlain et al., 2008; Remijnse et al., 2006). However, studies employing more complex versions of deterministic reversal learning tasks (e.g. by increasing the number of choices rather than using the simpler two-choice paradigm) report that adults with OCD commit more post-reversal errors than healthy controls indicative of impaired cognitive flexibility (Apergis-Schoute et al., in-prep; Endrass, Koehne, Riesel, & Kathmann, 2013). Additionally, a proportion of probabilistic reversal learning studies found that adult OCD patients commit more post-reversal errors and shift more following misleading negative feedback delivered by the 'correct' stimulus (a measure commonly known as shifing to spurious negative feedback) (Apergis-Schoute et al., in-prep; Endrass, Kloft, Kaufmann, & Kathmann, 2011). This implies that patients' responses are highly influenced by punishing or negative feedback. While no published research has explored reversal learning in paediatric OCD, one of the studies Dr. Julia Gottwald (a former PhD student in the University of Cambridge) presented in her doctoral thesis demonstrated that adolescents with OCD were unimpaired on deterministic reversal learning, but displayed more post-reversal errors on a probabilistic reversal learning task (Gottwald, 2017, thesis). However, adolescent patients did not

display significantly more shifting following spurious negative feedback during probabilistic reversal learning (Gottwald, 2017, thesis).

Lately, emerging research employing sophisticated computational models (which involve analysing trial-by-trial data to investigate latent decision-making processes such as feedback sensitivity and reward maximisation) has revealed adults with OCD actually present reduced choice consistency on probabilistic reversal learning tasks. Adults with OCD are more likely to select sub-optimal options (increased exploration) and are less likely to re-select options that were previously chosen (reduced perseveration) (Apergis-Schoute et al., in-prep; Kanen, Ersche, Fineberg, Robbins, & Cardinal, 2019). These results are at odds with adult patients' perseverative tendencies on other aforementioned cognitive flexibility tests, which may be attributed to the feedback on this type of task being probabilistic and thus promoting more uncertainty in decisions. Hitherto, no studies have examined probabilistic reversal learning in a sample of only paediatric patients with OCD, although one study has reported less perseveration on the task in a sample containing both adult and adolescent OCD patients (Hauser et al., 2017).

Summary

The majority of studies employing probabilistic and deterministic reversal learning tasks identify intact performance in adults with OCD, although patients show reduced lateral and medial OFC activation when completing the tasks. A few studies have also found evidence for adult patients to display increased perseveration on deterministic reversal learning tasks and more shifting to spurious negative feedback on probabilistic reversal learning tasks. The limited evidence available for child patients suggest intact deterministic reversal learning performance and impaired post-reversal performance on probabilistic reversal learning tasks, however more research is needed to draw firm conclusions. Computational modelling work demonstrates that adults with OCD make more exploratory and less perseverative choices on probabilistic reversal learning paradigms but it is hitherto unknown whether children with OCD show similar behaviour.

1.2.3 Response Inhibition

Response inhibition refers to the ability to inhibit a pre-potent motor response, and impairment in this domain has been suggested to account for OCD patients being unable to stop repetitive rituals (Chamberlain, Blackwell, Fineberg, Robbins, & Sahakian, 2005). Tasks used to study inhibition in children with OCD include the Stroop Colour and Word Test (often abbreviated to the Stroop test)

(Stroop, 1935), Stop-Signal Task (SST) (Logan, Cowan, & Davis, 1984), Go/No-Go (GNG) task, and the Continuous Performance Test (CPT).

The Stroop test entails reading different coloured words aloud and inhibition is measured via number of errors and reaction times when the word and the colour are incongruent (e.g. the word 'purple' written in the colour green). A few studies have found that children with OCD make more errors and have longer reaction times compared to healthy controls on the task (Baykal et al., 2014; Isik Taner et al., 2011; Yamamuro et al., 2017). Furthermore, SSRI treatment did not improve performance in unmedicated patients suggesting that inhibition deficits are stable and resistant to treatment (Yamamuro et al., 2017). A majority of the studies, however, found no behavioural deficits on the Stroop test (Andrés et al., 2007; Chang, McCracken, & Piacentini, 2007; Geller et al., 2018; Gruner et al., 2012; Ota et al., 2013). Surprisingly, young patients performed even better than controls in Beers et al.'s (1999) study. In spite of this, administration of this task alongside neuroimaging methods has shed light on key brain abnormalities in child OCD patients. Using functional near-infrared spectroscopy (fNIRs), patients displayed significantly reduced prefrontal haemodynamic activity during the Stroop test (Ota et al., 2013; Yamamuro et al., 2017). Abrnormal activity in young patients was present even in the absence of performance impairments (Ota et al., 2013). Specifically, changes in oxyhaemoglobin levels occurred more slowly in patients compared to controls in the frontopolar region of the prefrontal cortex, an area that is implicated in higher order cognitive control (Boschin, Piekema, & Buckley, 2015).

The GNG task, SST, and CPT generally measure the ability to inhibit a motor action following visual or auditory cues. Zandt et al., (2009) found that young OCD patients committed more inhibitory errors on a version of the SST known as the Walk-Don't-Walk, in which participants have to draw lines along a path with a pen until they hear a tone cueing them to stop. Furthermore, on an emotional GNG task, OCD patients made more false presses when cued to inhibit responses (Waters & Farrell, 2014). Likewise, patients in Baykal et al.'s (2014) study tended to make more errors of commission on the CPT. Woolley et al. (2008) reported that young boys with OCD under-recruited the bilateral OFC, right thalamus, and basal ganglia whilst completing a 'Stop Task', revealing an inhibitory control-related dysfunction in the cortico-striatal-thalamo circuit. However, other studies reported no underperformance or reaction time deficits on these tasks in children with OCD (Beers et al., 1999; Gooskens et al., 2018; Hybel, Mortensen, Lambek, Thastum, & Thomsen, 2017; Ornstein et al., 2010; M. S. Shin et al., 2008).

Similar to what was discussed in the cognitive flexibility domain, adults with OCD show profound deficits in behavioural inhibition despite such deficits being unpronounced in children with OCD. Namely, adults with OCD are impaired at inhibiting responses on the SST and GNG (Chamberlain, Müller, et al., 2006; Menzies et al., 2007; S. Morein-Zamir et al., 2013; Penadés et al., 2007) and make more errors of commission on the Stroop test (Peles, Weinstein, Sason, Adelson, & Schreiber, 2013; Penadés et al., 2007; Penadés, Catalán, Andrés, Salamero, & Gastó, 2005). Nonetheless, brain activity data is comparable between subtypes as adults with OCD also show reduced activation in bilateral OFC during inhibition tasks (Menzies et al., 2007; Page et al., 2009).

Summary

While there is some evidence for an inhibitory control deficit in children with OCD, the majority of studies do not describe significant impairments. Brain regions that seem to be associated with inhibitory control in children with OCD include the frontopolar cortex, OFC, thalamus, and basal ganglia.

1.2.4 Memory

Broadly, pertinent studies have investigated the following domains of memory in children with OCD: working memory, long-term verbal and non-verbal memory, and visuospatial memory.

Working memory involves temporary maintenance and manipulation of information and is thought to underlie broad cognitive impairments in many psychiatric disorders (Gold et al., 2018). Both children (Andrés et al., 2007; Geller et al., 2017; Hybel et al., 2017; Shin et al., 2008; Taner et al., 2011) and adults (Demeter et al., 2013; Krishna et al., 2011; Moritz et al., 2002; Tallis, Pratt, & Jamani, 1999) with OCD appear to have intact verbal working memory functioning, demonstrated by their proficiency on backwards digit span tests. Incidentally, Geller et al. (2017) proposed that children with OCD only show impaired working memory when under time pressure, as they found that patients performed poorly on a timed arithmetic test but not on the (non-timed) digit span test. More unconventional tests of working memory have also garnered interesting results; Chang et al. (2007) found patients performed poorly on a spatial working memory task known as the Finger Windows test (Sheslow & Adams, 2003), which requires participants to remember the sequential placement (by an examiner) of a pencil into a series of holes in a plastic card. Next, Wolff et al. (2017) administered a task switching paradigm where participants had to assess, on screen, whether a numerical target was smaller or greater than 5 or whether a target was even or odd. Patients performed worse on the working memory portion of the task which required remembering when to

switch tasks. This is indicative of children with OCD having specific deficits in visual working memory tasks but exhibiting intact verbal working memory measured via digit span.

Studies that assessed other memory domains show conflicting results. On the one hand, widespread memory impairments across verbal, non-verbal, and visuospatial memory tasks have been found in children with OCD (Andrés et al., 2007; Gottwald et al., 2018; Ornstein et al., 2010), but many papers also report no significant deficits in these domains (Beers et al., 1999; Chang et al., 2007; Geller et al., 2018; Hybel et al., 2017; Kim et al., 2018; Shin et al., 2008). This is in contrast to findings in adult patients, as two meta-analyses have reported a prominent non-verbal memory deficit with large effect sizes in adult OCD (Abramovitch, Abramowitz, & Mittelman, 2013; Shin, Lee, Kim, & Kwon, 2014). Garcia-Delgar et al.'s (2018) study provides fascinating insight into these opposing findings. Researchers administered various memory tests to 61 youths with OCD and divided the sample into 'selectively impaired' and 'globally preserved' groups based on their task performance. Visuospatial and non-verbal memory were most affected in the 'impaired' group while the 'preserved group' exhibited comparable performance to controls, indicating that youths with OCD can display vastly different presentations of memory ability. These discrete profiles could not be explained by demographic and clinical factors as there were no differences between the two groups on age, gender, OCD severity and medication status. Nonetheless, the 'selectively impaired' group comprised a very limited sample of 9 patients, which could undermine the reliability of these findings.

Two functional magnetic resonance imaging (fMRI) studies have clarified the brain activation profiles of paediatric OCD associated with memory ability. Diwadkar et al. (2015) found that children with OCD displayed aberrant activation of frontoparietal regions [dorsal prefrontal cortex (dPFC), parietal lobe, and middle frontal gyrus] that was modulated by dorsal ACC (dACC) activity during high and low working memory demands. The hyper-modulation by the dACC was proposed to reflect the inefficiency of control-related networks in paediatric OCD. Abnormal frontoparietal activation during working memory tests has also been reported in adults with OCD (De Vries et al., 2014). Another theory with regards to impaired memory is that children with OCD fail to employ cognitive strategies when encoding information (Batistuzzo et al., 2015). When asked to use a semantic clustering strategy to solve a Verbal Episodic Memory test, children with OCD revealed decreased activity in the bilateral dorsomedial PFC, superior frontal gyrus, right middle frontal gyrus, inferior parietal lobe, superior and middle temporal gyri and putamen (Batistuzzo et al., 2015). Moreover, semantic clustering scores correlated with episodic memory scores in controls but not patients. The authors concluded that altered neural mechanisms underlie strategy implementation in children with OCD, that could account for differences in memory ability reported in other papers.

Summary

Similar to other functions described, findings for a memory impairment in children with OCD are varied. Child and adult patients are not impaired on tests of verbal working memory such as the digit span test, but children with OCD may face difficulties specifically with visual working memory paradigms and timed tasks. In contrast, adults with OCD are mostly impaired on non-verbal memory tests. In addition, it was found that children with OCD can be divided into two discrete cognitive profiles, namely those with intact cognition and those with impaired visuospatial and verbal memory ability, which could explain disparities in the child OCD memory results. Finally, performance on various memory tasks in young patients seems to be driven by atypical activation of frontal, parietal, and striatal regions.

1.2.5 Decision-Making

Decision-making tasks generally test whether participants can make favourable choices with the aim of accumulating rewards, points or positive feedback. Three studies investigated decision-making using gambling tasks, namely the Iowa Gambling Task (IGT) (Bechara, Damasio, Damasio, & Anderson, 1994) and the Cambridge Gambling Task (CGT) (Rogers et al., 1999). On the IGT, subjects are presented with four decks of cards, each associated with different probabilities of gaining and losing points. Subjects have to learn over time to select cards from decks that are advantageous (offer points without high risk of losses). Kodaira et al. (2012) reported children with OCD made more disadvantageous selections on the IGT and correspondingly, Norman et al. (2018) found that children with OCD showed underactivation of the ventromedial OFC when choosing advantageous choices on the IGT relative to controls and children with Attention Deficit Hyperactivity Disorder (ADHD). Medial OFC underactivation has also been observed in adults with OCD when they adjusted behaviour according to feedback on a probabilistic reversal learning task (Remijnse et al., 2009). Along a similar vein, Norman et al. inferred that this underactivity displayed by children with OCD underlay impairments in learning from feedback and using stochastic information to guide their choices. Computational modelling of the data revealed that patients with OCD explored non-optimal decks more than other groups, suggesting a lack of confidence in their choices (Norman et al., 2018). Combined, results point towards OCD patients being intolerant of uncertainty, which is connected to possible OFC dysfunction (Norman et al., 2018). However, when tested on the CGT, children with OCD showed analogous performance to controls (Hybel et al., 2017). This is likely due to task differences; the IGT relies on implicitly learning to favour the deck that offers smaller rewards but

is less risky, while the CGT explicitly informs participants of choice pay-offs, and is considered a more straightforward test of risky decision-making. Hence, children with OCD show impaired decision-making under uncertainty but intact decision-making under risk. These results mirror that of adult patients who similarly display difficulty with ambiguous decision-making but are unimpaired on risky decision-making (Pushkarskaya et al., 2015; Viswanath, Janardhan Reddy, Kumar, Kandavel, & Chandrashekar, 2009). Moreover, difficulty with ambiguous decision-making may be consistent with aforementioned reduced perseveration and more exploration on probabilistic reversal learning tasks (where outcomes are also stochastic) displayed by adult patients (Apergis-Schoute et al., in-prep; Hauser et al., 2017; Kanen et al., 2019).

Two computational modelling studies reveal further evidence of uncertainty intolerance in children with OCD (Erhan et al., 2017; Hauser et al., 2017). Hauser et al. (2017) administered the Information Sampling Task (Clark, Robbins, Ersche, & Sahakian, 2006) requiring participants to guess whether the majority of (initially) hidden cards are green or yellow. Participants are allowed to turn over cards, one-by-one, to reveal the colour underneath before making their decisions. When not penalised for turning over cards, patients turned over more cards than controls and also made more accurate judgements. Bayesian modelling revealed that all participants felt increasing urgency to make a decision the more they turned over cards, but adolescent OCD patients discounted subjective costs of taking longer to make a decision, such as fatigue, impatience and time. Erhan et al. (2017) likewise employed a Dot Discrimination task, a low level perceptual decision-making task requiring participants to decide whether clusters of dots are moving towards the left or right on a screen, with varying noise levels. Modelling of these data showed that patients took longer to accumulate evidence, and showed increased duration between accumulating evidence and executing responses compared to controls. Both studies concluded that decision-making thresholds are abnormally high in paediatric OCD patients, reflecting their desire for certainty before making choices. Adults with OCD equally show cautious decision-making on perceptual decision-making tasks suggesting that certainty-seeking is a shared trait between subtypes (Banca et al., 2015). However, adults with OCD typically do not show increased information seeking on information sampling tasks (Chamberlain, Fineberg, Blackwell, et al., 2007; Morein-Zamir, Shapher, Gasull-Camos, Fineberg, & Robbins, 2020), suggesting an increased capacity to process evidence in adult subjects.

Summary

Decision-making is impaired in children and adults with OCD when task environments are noisy/stochastic or when they involve implicit learning (such as the IGT). This could be primarily

driven by patients having poor tolerance for uncertainty. In addition, adults and children with OCD display underactivation in the medial OFC on tasks with probabilistic feedback. Children with OCD also show significantly increased and slower information seeking on information sampling tasks but this behaviour is not prominent in adults with OCD.

1.2.6 Planning

Studies typically utilise "Tower" tests to investigate planning, which involve moving beads or disks from peg to peg with the aim of matching a model pattern as quickly as possible. These tests are considered planning tasks as it is assumed that planning a course of action is required to solve the task problems efficiently (Riccio, Wolfe, Romine, Davis, & Sullivan, 2004). The following tasks are commonly used to probe planning ability: Tower of London (TOL) (Shallice, 1982) (Shallice, 1982), Tower of Hanoi (TOH) (Kotovsky, Hayes, & Simon, 1985), Delis-Kaplan Executive Function System (D-KEFS) Tower Test (Delis, Kramer, Kaplan, & Holdnack, 2004) and Stockings of Cambridge (SOC) (Owen et al., 1995).

Compared to healthy controls, children with OCD require more moves to solve the SOC (Kim et al., 2018; Negreiros et al., 2019) and D-KEFS Tower Test (Ornstein et al., 2010), and used more time to solve the TOL (Huyser, Veltman, Wolters, De Haan, & Boer, 2010), revealing impaired planning ability. On the contrary, Hybel et al. (2017) and Beers et al. (1999) found equivalent performance across controls and patients on the SOC and TOH. However, Hybel et al. did not explicitly report response latencies in their analysis of the SOC, so we are unable to infer from their findings whether child patients showed slower planning on the task.

Intriguingly, Huyser et al. (2010) uncovered evidence for planning dysfunction being a state (a transient characteristic influenced by current environment), as opposed to a trait (a stable characteristic), feature of paediatric OCD. Brain abnormalities during planning, namely underactivation in the left posterior dorsolateral prefrontal cortex (dlPFC) and right parietal cortex, ceased to be statistically significant in patients following CBT treatment. Moreover, following treatment, patients were able to solve the task faster. This indicates that disrupted planning ability might be driven by symptom severity.

These findings are analogous to adults with OCD who are slower in completing the TOL and also show hypoactivation of the dlPFC during the task (Vaghi, Hampshire, et al., 2017). Moreover, although early studies report that CBT and even drug treatment are ineffective in remediating planning deficits in adult patients (Kuelz et al., 2006; Nielen & Boer, 2003), recent research has

found that planning deficits are improved following administration of SSRIs to adults with OCD (Lochner et al., 2020)

Summary

Children with OCD tend to react slower and require more moves to solve planning tests, similar to adults with OCD. Slow planning is also associated with underactivation of the dlPFC and parietal cortex, which normalises following CBT in children with OCD and following SSRI treatment in adults with OCD.

1.2.7 Action Monitoring

OCD has been frequently associated with overactive action monitoring, the generation of inappropriate error-detection signals, that gives rise to feelings of "wrongness" (Nieuwenhuis, Aston-Jones, & Cohen, 2005). Action monitoring is studied by examining an event-related potential component of the brain known as error-related negativity (ERN). ERN is generated by a fronto-central negative deflection that occurs 100ms after the execution of an incorrect response during forced-choice reaction time tasks (Endrass, Klawohn, Schuster, & Kathmann, 2008).

Studies have explored action monitoring in paediatric OCD using a combination of electrophysiological measures (electroencephalogram, EEG) or fMRI, and reaction time tasks such as the Flanker task (Eriksen & Eriksen, 1974), Multisource Interference Task (MSIT) (Bush & Shin, 2006), and the Simon's task (Simon & Wolf, 1963).

All pertinent EEG studies to date have reported enhanced ERN in paediatric and adult OCD patients, uncorrelated with symptom severity, medication status, or presence of co-morbid disorders (Carrasco, Harbin, et al., 2013; Carrasco, Hong, et al., 2013; Hajcak, Franklin, Foa, & Simons, 2008; Hanna et al., 2012, 2018, 2016; Liu, Hanna, Carrasco, Gehring, & Fitzgerald, 2014; Riesel, 2019). One study even showed that UFDRs of children with OCD also display increased ERN (Carrasco, Harbin, et al., 2013) hence promoting overactive action monitoring as a plausible endophenotype of paediatric OCD. fMRI studies equally report OCD-related elevated activation in key frontal brain regions following task errors or high conflict trials, namely the ACC/dorsal ACC (Kate Dimond Fitzgerald et al., 2010; Huyser, Veltman, Wolters, De Haan, & Boer, 2011) (Fitzgerald et al., 2010; Huyser et al., 2011), posterior medial frontal cortex (pMFC) (Fitzgerald et al., 2018, 2010), and dlPFC (Fitzgerald et al., 2013). Neural activity underlying action monitoring was furthermore found

to be unchanged following cognitive-behavioural treatment (Huyser et al., 2011), demonstrating the plausibility of this function as a trait marker.

One study investigated how abnormal action monitoring may manifest behaviourally. Liu et al. (2012) proposed that behavioural adaptation to conflicts/errors can be assessed by observing post-error slowing and post-conflict adaptation during reaction time tasks. Post-error slowing involves slowing down responses after an error in an effort to reduce future errors, while post-conflict adaptation involves speeding up following a correct response to an incongruent trial which indicates that participants have learnt to attend to relevant information. Compared to controls, youths with OCD did not display either of these adaptive responses during the MSIT, demonstrating deficits in adjustment of cognitive control when conflict is present. Poor cognitive control has also been noted as a feature of adolescent OCD (Gottwald et al., 2018) and in real life could contribute to patients feeling that they are ill-equipped to handle stressful or triggering situations, leading to hypothetical coping mechanisms such as avoidance or checking.

Summary

Overactive action monitoring, operationalised as increased ERN and abnormal activation in specific frontal regions (i.e the ACC) in response to errors is a stable trait of paediatric and adult OCD. Overactive monitoring could be linked to an inability to adapt behaviour following mistakes and/or demanding problems.

1.2.8 Habit-directed and goal-directed control

Actions are suggested to be regulated by two distinct systems. On one hand, the goal-directed system controls actions that are sensitive to the values of prospective outcomes, and rely on strengthening stimulus-response-outcome (S-R-O) associations. On the other hand, actions under the habit system are insensitive to such outcomes values, but instead are triggered automatically by the environmental stimuli/context and rely on the strengthening of stimulus-response (S-R) associations. While habitual responding is automatic and simple to execute, goal-directed responding requires complex reasoning and planning to attain a set-goal. These systems are suggested to work in conjunction to regulate behaviour (Balleine and Doherty 2010). In keeping with this account, OCD has been conceptualised as a disorder of maladaptive habit formation (Graybiel & Rauch, 2000) as affected individuals engage in seemingly habitual and purposeless rituals in the absence of any goal.

Outcome devaluation tasks and contingency degradation tasks are commonly used to probe the extent of reliance on habit and goal-directed policies. First, outcome devaluation tasks involve learning to make instrumental responses to different stimuli in order to receive a (typically) rewarding outcome. After overtraining, some stimuli become devalued or no longer deliver expected outcomes and subjects must withhold from responding to them. Strong habit formation is inferred if subjects continue to make responses to these devalued stimuli. Adults with OCD continue responding to devalued stimuli on outcome devaluation tasks under both appetitive and aversive contexts (Gillan et al., 2014, 2011) implying stronger habit-directed control and reduced goal-directed control. One study so far has administered an outcome devaluation task to adolescents with OCD and found poor instrumental learning of action-outcome associations in the training phase (Gottwald et al., 2018), which has not been reported in adult OCD studies. During devaluation, adolescent patients tended to respond more to devalued stimuli but also did not respond appropriately to still valuable trials. This suggests that adolescent patients show more of an impairment in action-outcome learning and retaining S-R-O associations in memory instead of a bias for habitual responding.

Next, contingency degradation tasks probe how behaviour is adjusted following changes in instrumental contingency. Subjects are instructed to respond to stimuli and assess how much their actions are predictive of an outcome. In some instances, actions are completely predictive of outcomes, whereas other times contingencies between actions and outcomes are degraded, meaning outcomes occur independent of action. Habitual responders are thought to continue instrumental responses even when action-outcome relationships are degraded. On this task, adults with OCD reportedly responded more than control subjects in situations when actions were not causal of outcomes (Vaghi et al., 2019), but adolescent patients do not show this inappropriate responding (Gottwald, 2017, thesis). Overall behavioural results from these two tasks point to reduced goal-directed control in adults with OCD while evidence is less forthcoming in youths with OCD.

Neural evidence is also in favour of an imbalance between goal-directed and habit-directed systems in adult OCD. A symptom provocation study (which involves triggering obsessions and urges in OCD using provocative images or videos, e.g. an image of an unattended stove) reported that adult OCD patients displayed underactivity in brain regions associated with goal-directed control (prefrontal-caudate areas) and overactivity in regions associated with habit-directed control (subthalamic nucleus and putamen) (Banca, Voon, et al., 2015). These results suggest that triggering compulsions activates the habitual system, supporting the notion that compulsions are rooted in habits. However, symptom provocation studies show different results in paediatric samples, wherein under provocation children with OCD show reduced activation in both habit and goal-directed

regions (Gilbert et al., 2009). In addition, young patients were found to display hyperactivity in the temporal poles following provocation (Jaspers-Fayer et al., 2019), which are thought to be involved in integrating visceral emotional responses with sensory input (Pehrs et al., 2017). From this, we can perhaps infer that a bias for habitual control drives compulsions in adults with OCD, but compulsions in children with OCD may be more driven by emotions such as stress or anxiety.

Next, model-based and model-free control are also often used as computational proxies for goal-directed and habit-directed behaviour respectively (but indeed they may not be completely equivalent (Miller, Shenhav, & Ludvig, 2019)). Model-based control is present when subjects are able to form an accurate model of an environment and adapt behaviour accordingly to maximise positive outcomes or avoid danger. A simple example of model-based behaviour would be understanding that one stimuli in a probabilistic reversal learning task is associated with a higher chance of rewarding outcomes, and directing all future responses to the stimulus in question. A model-free learner, by contrast, would be unable to learn the structure of the task and instead base responding purely on most recent feedback leading to more lose-shift and win-stay behaviour (Daw, Gershman, Seymour, Dayan, & Dolan, 2011). The two-step sequential decision-making task (Daw et al., 2011) is commonly used to disentangle model-based from model-free behaviour and is described in detail in Chapter 4 of this thesis. Adults with OCD typically show reduced model-based control on this task (Voon, Baek, et al., 2015; Voon, Derbyshire, et al., 2015; Wheaton, Gillan, & Simpson, 2019) perhaps due to an inability to employ sufficient goal-directed faculties to learn the complex task structure. To date, no studies have directly probed model-based and model-free behaviour in youths with OCD.

Summary

An imbalance between goal-directed control and habit directed systems, as well as reduced model-based behaviour has been well documented in adults with OCD, but not in children with OCD who may show more of an impairment with basic instrumental learning (Gottwald et al., 2018).

1.2.9 Meta-cognition

Meta-cognition describes an individual's accuracy in judging their own actions, thoughts, and abilities. Inaccuracies in meta-cognition have been suggested to drive compulsions (Rachman, 1993) wherein individuals with OCD overestimate how much control their intrusive thoughts have over themselves and the environment. For instance, they may often believe that having an intrusive thought is equivalent to the action or event happening in real life. Additionally, meta-memory

research suggests that adult patients' reduced confidence in memories during situations of high responsibility (for example, needing to check that stove knobs are off in order to prevent a fire) lead to increased certainty seeking and checking in adult OCD (Boschen & Vuksanovic, 2007; Hermans et al., 2008; MacDonald, Antony, MacLeod, & Richter, 1997; Tolin et al., 2001). However, there is less evidence for this behaviour in adolescents with OCD (Farrell, Waters, Boschen, & Milliner, 2011).

More recently, research suggests the impairment may not lie solely in inaccurate meta-cognition but in a dissociation between meta-cognition and actions. On the aforementioned contingency degradation task, adults with OCD continued to make responses during degraded phases despite having full awareness that degradation had taken place (Vaghi et al., 2019). Moreover, on outcome devaluation tasks, adults with OCD persist with responding even though they are aware that the stimuli are now devalued (Gillan et al., 2014). More convincingly, on a complex predictive-inference task (described in detail in Chapter 5 of this thesis) that was designed to test the strength of association between action and confidence in actions, adults with OCD were able to develop an accurate model of the stochastic task environment, indicated by confidence ratings, but they excessively changed their actions ignoring this knowledge. This dissociation between action and beliefs supports the notion that OCD is ego-dystonic in nature, in that patients understand their compulsions and worries are irrational but continue to partake in them.

In contrast, meta-cognition and its relationship to actions has not been as extensively studied in children with OCD, however, its existence can be inferred from other studies. For instance, on decision-making paradigms, child patients continuously sample information before making a decision even when sufficient information has already been acquired (Erhan et al., 2017; Hauser, Moutoussis, et al., 2017). In other words, young patients continue to request information even when doing so no longer has value within the context of the task. However, when tested on a contingency degradation task, adolescents with OCD showed intact knowledge of action-outcome contingencies and did not respond during degraded trials (Gottwald, 2017, thesis) suggesting actions and beliefs are not dissociated in young patients.

Summary

A dissociation between actions and beliefs is a plausible deficit in adult OCD which drives compulsive behaviour, but there is a lack of evidence supporting this in youths with OCD.

1.3 Overall summary and directions for thesis

Research thus far suggests that children with OCD are equivalent to adults with OCD on a few cognitive domains, including decision-making, action monitoring, planning, and some memory domains. However, there is less evidence for domains of cognitive flexibility, response inhibition, goal-directed vs. habit-directed control, and meta-cognition. Moreover, it is thought that adolescent OCD is more linked to a learning deficit as young patients show impaired rule and instrumental learning on cognitive flexibility and outcome devaluation tasks (Gottwald et al., 2018) which are not difficulties reported in adult OCD studies. This is indicative of a cognitive divergence between sub-types and that more research needs to be invested in understanding the cognitive framework of paediatric OCD as it is apparent that not everything known in adults with OCD can be applied to children with the disorder. Despite heterogeneous behavioural findings, children and adolescents with OCD show similar patterns of brain activity to their adult counterparts on various cognitive paradigms, namely reduced activity in frontal regions encompassing the OFC and dlPFC during flexibility, memory, inhibition, and decision-making tasks as well as increased activity in ACC during conflict monitoring tasks. This suggests that brain areas underlying cognitive domains are already functionally abnormal in paediatric OCD but behavioural deficits only become pronounced in adulthood.

1.3.1 Learning and decision-making

Impairments in learning and decision-making outlined so far may be driving young patients' poor performance and difficulty in concentrating in school settings (Negreiros et al., 2018; Piacentini et al., 2003), indicating research urgently needs to prioritise these domains. Evidence from decision-making research suggests adult and child patients alike partake in aberrant evidence accumulation and exploration in situations particularly when task environments are uncertain or stochastic (Banca, Vestergaard, et al., 2015; Erhan et al., 2017; Norman et al., 2018; Pushkarskaya et al., 2015; Viswanath et al., 2009). Adding to this, recent computational work suggests that adults with OCD display significantly reduced choice perseveration on probabilistic reversal learning paradigms (Apergis-Schoute et al., in-prep; Hauser et al., 2017; Kanen et al., 2019). Nonetheless the learning impairment may be even more pronounced in adolescents with OCD as their instrumental learning is impaired even on tasks that offer deterministic feedback such as the ID/ED task (Gottwald et al., 2018). Hence, to gain a holistic picture of atypical learning and decision-making in youths with OCD the experiments conducted in this thesis employed various paradigms that either offer probabilistic (Chapters 4-6) or deterministic feedback (Chapters 2-3) which will be described further on.

1.3.2 Feedback sensitivity

In addition to whether paradigms are probabilistic or deterministic, feedback valence (whether feedback is positive or negative) may also play a role in impaired learning and decision-making. Goal-directed control in adult OCD appears to be reduced regardless of valence (Gillan et al., 2014, 2011), while goal-directed control has only been probed in an appetitive (rewarding) context in adolescents with OCD (Gottwald et al., 2018). Intriguingly, other learning paradigms offer evidence for abnormal processing of negative feedback and errors in adult OCD. Abnormal anterior cingulate cortex signalling has been detected in adults with OCD in response to prediction errors, which describe the mismatch between expectations and real-life outcomes (Hauser et al., 2017; Murray et al., 2019). Furthermore, adults with OCD also display reduced activation in medial and lateral OFC during probabilistic feedback processing (Remijnse et al., 2009). Behaviourally, adults with OCD are reported to switch choices excessively on a PRL task in response to negative feedback (Endrass et al., 2011), and also update actions excessively following prediction errors (Vaghi, Luyckx, et al., 2017). Oversensitivity to negative feedback and intolerance of prediction errors is compatible with the robust finding of enhanced ERN following conflict detection in OCD (Riesel, 2019) and may be a factor driving learning and decision-making impairments. Moreover, it is in line with traditional theories of OCD suggesting avoidance of harm drives compulsive behaviour (Rasmussen & Eisen, 1990, 1992). In fact, youths with OCD typically report high levels of harm avoidance in daily life (Bey et al., 2017; Cervin, Perrin, Olsson, Claesdotter-Knutsson, & Lindvall, 2020; Ecker & Gönner, 2008; Ettelt et al., 2008).

However, recent computational studies of probabilistic reversal learning report no evidence of punishment oversensitivity in adults with OCD (Apergis-Schoute et al., in-prep; Hauser et al., 2017; Kanen et al., 2019). Instead, prominent punishment avoidance may be more pronounced in adult patients on deterministic tasks (Apergis-Schoute et al., 2017; Gillan et al., 2014; Morein-Zamir et al., 2013; Nielen, Den Boer, & Smid, 2009). Children with OCD, by contrast, show no abnormal punishment sensitivity on both probabilistic and deterministic tasks (Gottwald, 2017, thesis; Norman et al., 2018). Hence, it is uncertain whether feedback processing is disrupted in child-OCD as it may be in adult-OCD.

To assess the possibility that abnormal feedback processing contributes to poor learning and decision-making in youths with OCD in this thesis, computational models were fit to data from various learning tasks that are able to weigh the relative contribution of negative and positive feedback towards updating values associated with competing choices in Chapters 2,4, and 6. Furthermore, as goal-directed control in aversive contexts has not yet been investigated in youths

with OCD, an aversive paradigm probing Pavlovian-to-Instrumental Transfer (PIT) (described further below) was administered in Chapter 3.

1.3.3 Other cognitive processes

While the focus of this thesis is directed towards understanding why learning and decision-making are abnormal in youths with OCD, the tasks employed are sufficiently complex to enable insight into various cognitive processes. For instance, in Chapter 4, a sequential decision-making task is used to investigate model-based reasoning, exploitative vs. exploratory decision-making, and evidence accumulation. Model-based reasoning, in particular, has not been directly probed in paediatric OCD despite evidence overwhelmingly suggesting adults with OCD rely on model-free decision-making strategies (Voon, Baek, et al., 2015; Voon, Derbyshire, et al., 2015; Wheaton et al., 2019). Moreover, in Chapter 3, I utilise a Pavlovian-to-Instrumental paradigm to probe instrumental and Pavlovian processing, as implicit and explicit learning are thought to be disrupted in youths with OCD (Gottwald et al., 2018; Vloet et al., 2010). In parallel, the task also enables indirect inference of model-based and model-free mechanisms via examining how well subjects can integrate Pavlovian and instrumental influences to inform behaviour (see Chapter 3 for further explanation of this task). Difficulty in integrating Pavlovian and instrumental information is thought to be linked to reduced OFC control over striatum (Balleine & O'Doherty, 2010), and indeed as mentioned earlier, aberrant lateral and medial OFC activity has been detected in both youths and adults with OCD. Next, in Chapter 5, I administered a predictive-inference task originally employed by Vaghi et al. (2017) to understand the interplay between confidence and action in adults with OCD. The task has a probabilistic structure and involves using feedback and accumulating evidence over time to learn to position a 'bucket' on-screen in a location where a 'coin' is most likely to land. At the same time subjects have to rate how confident they are in their predictions of where the coin will land. Hence, this task not only probes learning and evidence accumulation, but also enables investigation of meta-cognition which is found to be dissociated from action in adults with OCD (Vaghi et al., 2019; Vaghi, Luyckx, et al., 2017). Through these tasks, I hoped to deduce a comprehensive framework of learning and decision-making in youths with OCD as well as further current understanding of other potentially disrupted cognitive processes such as model-based/goal-directed control and meta-cognition.

1.3.4 Focus on Adolescence

For various reasons, which will be outlined in this section, the studies in this thesis employed samples of adolescents with OCD and age-matched controls, ranging in age from 12-19 years.

Firstly, research into cognition in child-OCD so far employ samples with large age ranges, ranging from early childhood to late adolescence. For instance, participants in the studies of Hybel et al. and Lewin et al. were between 7-17 years old (Hybel et al., 2017; Lewin et al., 2014), while participants were between 7-18 years in Andres et al.'s (Andrés et al., 2008) and between 6-16 years in Shin et al.'s (Shin et al., 2008) studies. As mentioned in Section 1.1, clinical presentation of OCD appears to alter with age, and it is likely that cognitive characteristics associated with the disorder shift from early childhood to adolescence as well. Wide age ranges employed by past studies make it difficult to account for this heterogeneity. Hence, this thesis focused on an adolescent sample aged between 12 and 19 years. Alongside this reason, Gottwald et al. (2018) who uncovered significant learning impairments associated with juvenile-OCD also employed this age range. Hence, it is cogent that the same age range is used to understand the mechanisms driving this learning impairment. Furthermore, an added advantage to employing a fully adolescent sample is one of practicality: it is simply easier to recruit adolescents for research purposes as opposed to younger children who require more extensive approval procedures from ethics bodies, schools, and parents.

The most important rationale for this thesis' focus on adolescence is that adolescent development is a highly fascinating area of study, characterised by noteworthy physical, psychological, and neurological changes. This developmental stage is termed a sensitive period as significant brain and personality changes make adolescents susceptible to various psychiatric disorders (Kessler et al., 2005). Moreover, such biological changes drastically affect cognitive and executive functioning in healthy adolescents. Maturation of the adolescent brain is influenced by hormonal fluctuations during puberty (Arain et al., 2013), whereby surges in sex hormones affect the development of the limbic circuitry including the ventral striatum and amygdala (Crone & Dahl, 2012; Spear, 2000). Crone & Dahl (2012) propose that this results in more emotional or affective influence over goal-directed control, translating to increases in novelty-seeking, sensation-seeking and a tendency to process status-relevant social stimuli (for example, receiving attention and admiration from peers) as having increased motivational salience. Neuroimaging experiments have further uncovered key neural signatures within the adolescent brain. Grey matter volume in the prefrontal-cortex, a region important for top-down control of behaviour, has been reported to follow a U-shape trajectory, peaking at pre-adolescence, declining at the onset of adolescence, and increasing once again with age (Giedd et al., 1999; Gogtay et al., 2004). This decline has been suggested to underlie poor cognitive control in adolescents, resulting in increased risk-taking and impulsivity (Blakemore & Robbins, 2012). Moreover, a recent resting state fMRI study revealed that functional connections between cortical and subcortical regions are 'disruptive' in healthy adolescents; connections that were weak

at age 14 years were stronger by age 26 and connections that were strong at age 14 became weaker by age 26, indicative of developmental brain reorganisation (Váša et al., 2019). Authors speculate that this disruption is crucial for facilitating the development of adult mental faculties. Studies employing cognitive tasks alongside fMRI methods are also highly informative, revealing adolescents, but not adults, have heightened activity in limbic and striatal regions during reward processing and when evaluating uncertain pay-offs associated with decisions (Silverman, Jedd, & Luciana, 2015; Van Leijenhorst et al., 2010). These brain functional differences can explain several findings reported in behavioural cognitive research, whereby adolescents, compared to adults, are more sensitive to punishing feedback on learning tasks (Hauser et al., 2015; Rodriguez Buritica et al., 2019; Rosenbaum, Grassie, & Hartley, 2020; van den Bos et al., 2012), display reduced goal-directed decision-making (Decker, Otto, Daw, & Hartley, 2016), and have difficulty integrating appetitive and aversive feedback on probabilistic learning tasks (Palminteri, Kilford, Coricelli, & Blakemore, 2016).

Thus, it is interesting to ponder how OCD, a disorder associated with widespread brain (Piras et al., 2015) and executive (Abramovitch, Abramowitz, & Mittelman, 2013) dysfunction interacts with the significant biological and cognitive changes occurring during adolescence. Could this be a major reason for the cognitive distinctions between adult and juvenile-OCD? Moreover, equivalent performance between adolescents with and without OCD found across several cognitive domains may be due to the ongoing development of such functions in healthy adolescents. OCD may impair or stunt healthy maturation of said functions, leading to marked deficits in adulthood but not adolescence.

1.3.5 Medication

Next, a limited proportion of the paediatric OCD studies reviewed investigated the effects of medication on cognitive performance. One of the studies that has reported that SSRI treatment successfully improved not only disorder symptoms but also performance on various cognitive domains in paediatric OCD (Andrés et al., 2008), which is consistent with findings from adult OCD studies (Lochner, Chamberlain, Kidd, Fineberg, & Stein, 2016; Lochner et al., 2020; Palminteri, Clair, Mallet, & Pessiglione, 2012). However, another study suggests that children with OCD medicated with SSRIs underperform on the WCST compared to medication-naïve child patients (Gruner et al., 2012). Thus, to understand the effects of SSRI medication on learning and decision-making in adolescent OCD, each experimental chapter contains a section analysing whether medication status influences task performance.

1.3.6 Computational Modelling

The majority of studies that have probed cognition in youths with OCD employed standard frequentist statistical methods to analyse performance data from computerised tasks. At times, it can be inappropriate to draw strong conclusions from these types of analysis as standard cognitive tasks are often complex and lack specificity due to them probing many different functions simultaneously (Marzuki, Pereira de Souza, Sahakian, & Robbins, 2020). For example, the WCST is a complex task, tapping into visual search, learning from positive and negative feedback, exploration, attention, and potentially working memory as participants have to retain 3 different rules in memory and switch between rules accordingly. Hence, researchers using standard statistical tests that typically only capture differences in averaged individual data may fail to capture more distinct deficits in cognition.

Lately, adult OCD studies have successfully utilised computational modelling methods to dissociate latent decision-making processes in cognitive tasks (Banca, Vestergaard, et al., 2015; Hauser et al., 2017; Kanen et al., 2019; Mandali, Weidacker, Kim, & Voon, 2019; Voon, Derbyshire, et al., 2015). Modelling involves formulating a mathematical function equipped with different parameters of interest to analyse trial-by-trial data. Commonly used parameters in neurocognitive computational models include the learning rate (the extent to which new incoming information influences subsequent choices), perseveration/stickiness (how often choices are repeated), and inverse temperature (how often are more favourable/valuable choices chosen). Values of these parameters are estimated when a computational model is fit to participants' data, enabling quantification and classification of behaviour. A simple, elegant model of reinforcement learning is the Rescorla-Wagner model (Wagner & Rescorla, 1972) which was originally conceptualised to capture how strongly a conditioned (CS) was predictive of unconditioned stimulus (US) stimulus (termed associative strength) and how this changes over time (see Equation 1.1).

$$V_{t+1} = V_t + \alpha(R_t - V_{total}) \text{ – Equation 1.1}$$

Key: V = value function; t = trial; R = outcome; α = learning rate

In the Rescorla-Wagner model above, V_t (value function) represents the current associative strength between a CS and a US (at trial t). In other words, V_t represents how strongly a CS is predictive of a US. In order to calculate the CS-US strength in the subsequent trial (V_{t+1}), V_t is added to the prediction error, $R_t - V_{total}$, which is essentially the total CS-US strength (V_{total}) subtracted from an outcome (R_t) representing whether the CS and US are contingent in trial t (1 if US-CS are contingent and 0 if they are not contingent). If R_t is 1 (meaning US and CS are contingent), the US-CS strength will increase for the next trial. The prediction error is controlled by

the parameter α (learning rate), which determines how much an immediate outcome, R, influences the associative strength value, V. If α is 1, R completely influences a change in the CS-US strength. Inversely, as α approaches 0, immediate outcomes are less influential in changing the CS-US strength. This algorithm and many others are widely used in human and animal research to model learning. For instance, it can be used to understand how subjects learn to associate one stimulus (CS) with a higher chance of positive feedback (US) in probabilistic reversal learning tasks. More recently, reinforcement learning models have been employed to understand how psychiatric and neurological disorders disrupt otherwise healthy learning processes.

Computational modelling methods are advantageous for understanding the factors that most affect learning in youths with OCD. For example, by fitting the Rescorla-Wagner model containing the learning rate parameter (α) to data, we can decipher whether a subject tends to adapt the value function associated with a choice (termed 'choice value') based on most recent feedback or otherwise discounts recent feedback in favour of information accumulated over time. To-date, only 3 cognitive paediatric OCD studies have employed computational modelling techniques (Erhan et al., 2017; Hauser, Moutoussis, et al., 2017; Norman et al., 2018). Nevertheless, findings from these studies have illuminated how youths with OCD make decisions, namely through increased exploration and higher decision-making thresholds. Hence, computational modelling is a viable method for understanding underlying learning and decision-making processes in youths with OCD, a feat which has proven elusive in studies employing standard analyses of cognitive performance. In Chapters 2,4,5, and 6 I fitted computational models to cognitive task data in order to disentangle these various latent processes.

1.4 Overview of Experimental Chapters

The overall aim of this thesis is to understand mechanisms contributing to atypical learning and decision-making in adolescents with OCD. I also sought to understand whether well-researched domains thought to be driving compulsions in adult OCD are equally impaired in adolescent-OCD, namely reduced goal-directed/model-based reasoning and a dissociation between meta-cognition and action. To achieve this, a battery of cognitive tasks probing learning and decision-making was administered to juvenile patients with OCD and age/gender-matched healthy controls, culminating in 5 different studies. Computational modelling was implemented in 4 out of 5 experimental chapters to gain greater insight into the complex processes contributing to learning and decision-making.

Chapter 2: Mechanisms Underlying Performance on Well-Known Task of Cognitive Flexibility in Adolescent OCD

Research generally concludes limited evidence for a cognitive flexibility deficit in youths with OCD. Nonetheless, some of the reviewed studies utilising cognitive flexibility tasks found impairments not related to flexibility, suggesting other factors are driving performance on these tasks. Thus, this study aimed to investigate the latent processes driving adolescent-OCD performance on a commonly used task of cognitive flexibility, namely the WCST. Twenty-three adolescent patients and 46 healthy adolescents were assessed on a computer-based version of this task. Bayesian hierarchical models were used to disentangle trial-by-trial performance of each group. The following model parameters were extracted: reward sensitivity, punishment sensitivity, decision-consistency, and attention to feedback. I predicted adolescent patients would show altered feedback sensitivity and decision-consistency on the task, consistent with adult and paediatric studies reporting abnormal exploration and feedback processing in patients with OCD.

Chapter 3: Pavlovian-to-Instrumental Transfer in Adolescents with OCD

Evidence suggests that children and adolescents with OCD are impaired at conducting implicit (Pavlovian) and explicit (instrumental) learning (Gottwald et al., 2018; Vloet et al., 2010). Additionally, goal-directed and model-based reasoning are reduced in adults with OCD (Gillan et al., 2014, 2011; Voon, Derbyshire, et al., 2015), and there is also evidence for patients showing enhanced sensitivity to negative feedback and excessive avoidance of harm (Apergis-Schoute et al., 2017; Endrass et al., 2011). Therefore, this study aimed to investigate whether instrumental and Pavlovian

processing were impaired in adolescents with OCD specifically under aversive contexts using a Pavlovian-to-Instrumental transfer paradigm. I also aimed to understand whether adolescents with OCD could successfully integrate learnt instrumental and Pavlovian influences to guide behaviour, which would be indicative of intact model-based control. The task was administered to 19 adolescents with OCD and 20 healthy controls. I hypothesised that adolescent patients would show reduced initial Pavlovian and instrumental learning which would contribute to reduced Pavlovian-to-instrumental transfer later on.

Chapter 4: Model-Based Decision-Making in Adolescents with OCD

This study sought to understand model-free and model-based reasoning in youths with OCD (which is reported to be imbalanced in favour of model-free reasoning in adults with OCD) using a gold-standard task for delineating between the two types of learning styles, namely the sequential decision-making task (Daw et al., 2011). A child-friendly version of the task was administered to 20 adolescents with OCD and 20 healthy adolescents. Task performance was modelled using a reinforcement learning drift diffusion model which took into account participant choices and reaction times. I predicted that adolescents with OCD would present significantly reduced model-based decision-making in line with findings from adult OCD research.

Chapter 5: Meta-Cognition in Adolescent OCD: Are action and confidence dissociated?

Difficulty relying on action-outcome knowledge in decision-making is thought to be one of the factors driving compulsions in OCD. This has been shown empirically; on a predictive-inference task, adults with OCD updated their self-reported confidence levels according to changes in the task environment, but their actions disregarded this knowledge errors (Vaghi, Luyckx, et al., 2017). Hence, in this study, I aimed to uncover whether adolescents with OCD also display this confidence-action dissociation when making decisions. The same predictive-inference task used by Vaghi, Luckyx et al. was administered to 23 adolescents with OCD and 46 healthy adolescents. A Bayesian learner model, also conceptualised by Vaghi, Luyckx et al., was used as a benchmark for ideal behaviour. Regression models were constructed to test how different parameters in the Bayesian model influence participants' performance. A separate regression model was then constructed to understand the strength of the relationship between action and confidence in the task. I hypothesised that adolescents with OCD would display a significant dissociation between actions and confidence similar to adult patients.

Chapter 6: Probabilistic Reversal Learning in Adolescents with OCD

Recent computational work suggests that adults with OCD show reduced perseveration and abnormal exploratory decision-making on probabilistic reversal learning tasks. Thus, the focus of this study was to assess whether adolescents with OCD display similar patterns of behaviour. A probabilistic reversal learning paradigm (Murphy, Smith, Cowen, Robbins, & Sahakian, 2002) was administered to 50 adolescents with OCD and 53 healthy volunteers. The task contained two stimuli, one with an 80% chance of providing positive feedback and one with only a 20% chance of positive feedback. The contingencies reversed halfway through the task. Trial-by-trial performance was modelled using a reinforcement learning model with the parameters reward sensitivity, punishment sensitivity, reinforcement sensitivity (exploitation), and stimulus stickiness (perseveration). I hypothesised that adolescents with OCD would display reduced perseveration and increased exploration in line with findings from adult OCD research.

1.5 Overall Sample

In total, 23 patients diagnosed with OCD were recruited via Child and Adolescent Mental Health Services, independent charities, as well as advertisements placed around Cambridgeshire and on social media. To qualify for the study, those in the OCD group had to meet DSM-V-TR (Diagnostic and Statistical Manual of Mental Disorders-V-Text Revision) diagnostic criteria for OCD, OCD must be their primary diagnosis, and they must score 12 or above on the Children's Yale-Brown Obsessive Compulsive Scale (Scahill et al., 1997). Apart from OCD, other significant Axis I mental disorders as diagnosed according to DSM-V-TR criteria including psychosis, bipolar disorder, anxiety disorder other than OCD, Tourette's Syndrome, Attention-Deficit Hyperactivity Disorder, Autism Spectrum Disorders, and eating disorders were exclusion criteria for this study. Severe physical impairments affecting eyesight or motor performance were also exclusion criteria, as they were predicted to affect performance on the tasks. Patients were screened by an experienced psychiatrist in an extended clinical interview supplemented by the Mini International Neuropsychiatric Interview [MINI for participants over 18, MINI-KID for participants under 18 (Sheehan et al., 1998, 2010)].

Fifty healthy controls in total were recruited via advertisements in state secondary schools around Cambridgeshire, local advertisements around Cambridge town, and via online job posting websites (e.g. Gumtree). They were screened using the age-appropriate MINI by an experienced psychology student to ensure they had no history of neurological or psychiatric illness. Precise information on the number of potential participants screened, excluded, and recruited are present in Figure 1.1.

Potential participants with OCD were thoroughly screened for comorbidities while controls were screened for any psychiatric disorder to enable investigation of the pure effects of adolescent-OCD on learning and decision-making, unconfounded by symptoms associated with other psychiatric conditions.

All participants were aged between 12 and 19 years and were fluent in English. This study was approved by the East of England - Essex Research Ethics Committee (REC 10/H030149/49). All volunteers gave written informed consent before beginning testing and received monetary compensation for their participation. If participants were under 16 years old, parental consent was also obtained. Participants were compensated at the rate of £8 an hour for contributing their time to the study.

Not all participants recruited were able to complete every cognitive task administered for this study. This is because the original study conceptualised for this thesis comprised the Wisconsin Card Sorting Test, predictive-inference task, and two other tasks that were discontinued in the end. Forty-

one controls and 7 patients participated in the original study but only 12 controls and 4 patients returned for the final version of the study consisting of the Wisconsin Card Sorting Test, PIT task, sequential decision-making task, predictive-inference task, and probabilistic reversal learning task. Hence, an additional 9 controls and 16 patients were recruited for the final study. Moreover, an extra 30 adolescent patients and 32 adolescent controls who had completed the same probabilistic reversal learning paradigm I have used, but in a past study (Gottwald, 2017, thesis), were added to the current sample of participants in Chapter 6. Sample sizes therefore vary from task to task, and each experimental chapter contains a unique description of the sample and their demographic details.

In the Statistical Analyses and Results sections of all studies presented in this thesis, the group including adolescents with OCD and the healthy control group are referred to as OCD and CTL respectively. When investigating the effects of medication, the medicated OCD group and unmedicated OCD group are referred to as MED+ and MED- respectively.

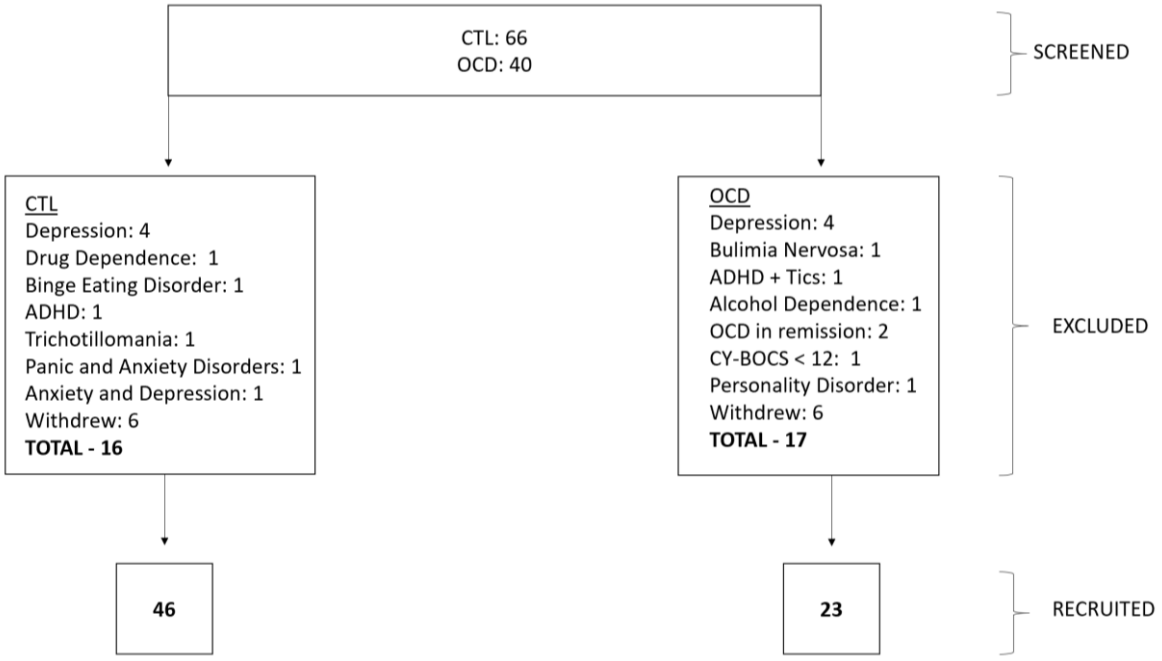

FIGURE 1.1: SCREENING AND RECRUITMENT DETAILS FOR OVERALL SAMPLE. KEY- CTL: CONTROL GROUP; OCD: PATIENT GROUP; ADHD: ATTENTION DEFICIT HYPERACTIVITY DISORDER; CY-BOCS: CHILDREN'S YALE-BROWN OBSESSIVE COMPULSIVE SCALE.

1.6 Clinical and Cognitive Questionnaires

To obtain a measure of anxiety and depression, participants completed the Beck Anxiety Inventory for Youth and the Beck Depression Inventory for Youth (Beck, Beck, & Jolly, 2005). Self-reported

obsessive-compulsive traits were assessed using the Obsessive-Compulsive Inventory-Revised (OCI-R) (Foa, Kozak, Salkovskis, Coles, & Amir, 1998). OCD symptom severity was also assessed with the Children's Yale-Brown Obsessive Compulsive Scale (Scahill et al., 1997). IQ measures were obtained using the Wechsler's Abbreviated Scale of Intelligence, Second Edition (WASI-II) (Wechsler, 2011). The Full-Scale IQ-2 subtests (FSIQ-2) from the WASI-II were used in these studies, comprising the Vocabulary and Matrix Reasoning tests. Lastly, the digit span subtest, consisting of forward and backward digit span, from the Wechsler's Intelligence Scale for Children, Fourth Edition (WISC-IV) (Wechsler, 2003) was used to assess verbal memory span and working memory span.

1.6.1 Statistical Analysis of Questionnaires (for all studies)

Questionnaire scores were analysed in the same way in every experimental chapter. Levene's test was used to assess homogeneity of variance while the Shapiro-Wilke's test was used to assess normality. When comparing OCD and CTL, clinical and IQ questionnaires were analysed using independent samples t-tests. When homogeneity of variance was violated, Welch's independent samples t-test was used. When data did not follow a normal distribution the two-sample Wilcoxon test was implemented. When comparing MED+, MED-, and CTL, one-way ANOVAs were conducted, followed by pairwise post-hoc t-tests with Bonferroni correction if significant main effects of group were detected. The Kruskal-Wallis test for main effects and post-hoc Dunn tests with Bonferroni correction for pairwise comparisons were implemented when homogeneity of variance and/or normality assumptions were violated.

Chapter 2: Mechanisms Underlying Performance on Well-Known Task of Cognitive Flexibility in Adolescent OCD

2.1 Introduction

The Wisconsin Card Sorting Test (WCST) is a commonly used test of executive function, used for assessing cognitive flexibility and is found to be sensitive to frontal lobe impairment (Anderson, Damasio, Jones, & Tranel, 1991; Robinson, Heaton, Lehman, & Stilson, 1980). Adults with OCD typically perform sub-optimally on the WCST and other cognitive flexibility tasks, such as the IDED task, TMT-B, and task switching tests (see Abramovitch et al., 2013 for meta-analysis). Impaired set-shifting (or increased perseverative errors) is thought to be the primary deficit displayed by adult OCD patients on these tasks, as patients show difficulty diverting attention from well-learnt rules that are no longer relevant, in favour of new, now relevant, rules. Cognitive inflexibility is thought to be intertwined with OCD symptomatology, as patients' compulsions in daily life are performed according to highly rigid rules. Moreover, even healthy populations with genetic and environmental risk for the disorder, namely first-degree of relatives of patients, show inflexibility on set shifting tasks (Chamberlain et al., 2007; Ozcan, Ozer, & Yagcioglu, 2016; Rajender et al., 2011), leading to cognitive inflexibility being regarded a possible endophenotype of OCD (Chamberlain & Menzies, 2009).

However, a recent meta-analysis of 75 studies, assessing effect sizes from a variety of set-shifting tasks (WCST, IDED,TMT-B, probabilistic reversal learning task) administered to adult patients found no strong evidence for a pure cognitive flexibility deficit associated with OCD (Fradkin, Strauss, Pereg, & Huppert, 2018). Within the WCST, effect sizes of perseverative errors overlapped with effect sizes of non-perseverative errors, while in probabilistic shift tasks, perseverative errors showed low effect sizes. This suggests that OCD is linked to general underperformance on set-shifting tasks, and not a specific flexibility impairment. Authors theorised that increased errors on the tasks are attributed to overcomplicated exploration, where patients attempt to evaluate too many possible rules at once, or perhaps a failure to process and learn from feedback. Nonetheless, this study did not compare flexibility scores on the IDED task with any control subscores, so they were unable to conclude whether adult patients showed a cognitive flexibility deficit exclusively on this task. Another meta-analysis focused on adult OCD performance on the IDED task (Chamberlain et al., manuscript submitted) compared performance on the intra-dimensional stage (IDS, where participants must learn to shift attention between different stimuli from one exemplar, e.g. lines, while distractor stimuli from an irrelevant exemplar

are introduced, e.g. shapes) with performance on the extra-dimensional stage (EDS, which involves shifting attention from a previously relevant exemplar to a new one, e.g. switching from lines to shapes). Thus, IDS was used as a control measure against the EDS flexibility measure. The meta-analysis unveiled a robust EDS performance impairment in adult patients, but no strong IDS impairment, suggesting that adult patients are indeed predominantly inflexible when it comes to switching between different categories but are able to flexibly switch responses between stimuli from the same category. Results from these two meta-analyses collectively indicate that inflexibility may be a characteristic of adult OCD, but evidence for this appears to be task and measure dependent. Furthermore, alongside or instead of cognitive inflexibility, underperformance on set shifting tasks may also be driven by overactive exploration and/or poor feedback learning.

Findings from cognitive flexibility studies involving paediatric OCD patients are even more heterogeneous. On the WCST, young patients are reported to be more perseverative, commit more overall errors, and complete fewer categories compared to healthy controls (Baykal et al., 2014; Isik Taner et al., 2011; Shin et al., 2008), with one study even reporting young patients committing exclusively more non-perseverative errors than healthy subjects (Andrés et al., 2007). Moreover, in contrast to findings from adult OCD research, paediatric patients have been found to commit more pre-EDS errors on the IDED task (Gottwald et al., 2018). These mixed findings denote that child-OCD is not associated with a clear flexibility deficit. In fact, as described in Chapter 1, majority of studies employing set-shifting tasks do not find differences in performance between young patients and controls (Andrés et al., 2007; Beers et al., 1999; Garcia-Delgar et al., 2018; Geller et al., 2018; Gruner et al., 2012; Hybel et al., 2017; Kim et al., 2018; Kodaira et al., 2012; Negreiros et al., 2019; Ornstein et al., 2010; M. S. Shin et al., 2008; Wilton et al., 2020).

These varied findings indicate that specific impairments on set shifting tasks are latent and unobservable using traditional group-based statistics. The WCST in particular is a complex task, tapping into visual search, learning from positive and negative feedback, exploration, attention, and potentially working memory as participants have to retain 3 different rules in memory and switch between them accordingly (Marzuki et al., 2020). To disentangle some of these latent processes driving WCST performance, cognitive scientists increasingly utilise computational models. The most well-known set of computational models for this purpose have been developed by Bishara et al. (2010), and contain parameters accounting for reward learning, punishment learning, decision-consistency, and attentional focusing (see Methods section of this chapter). The parameters have been validated and found to correlate highly with typical WCST summary measures such as perseverative errors, non-perseverative errors, and categories completed.

This modelling approach has been used to successfully reveal implicit cognitive strategies employed by various neuropsychiatric patient groups, among them individuals with substance dependence (Bishara et al., 2010), prefrontal cortex lesions (Gläscher, Adolphs, & Tranel, 2019), and schizophrenia (Farreny et al., 2016). Such an approach to analysing WCST performance has yet to be implemented in research involving patients with OCD.

As discussed in the introductory chapter of this thesis, studies employing computational modelling have found overactive exploration on decision-making tasks in youths with OCD (Erhan et al., 2017; Hauser, Moutoussis, et al., 2017; Norman et al., 2018). Similarly, it is interesting to speculate whether these features also influence performance on a cognitive flexibility task such as the WCST.

In this study, I sought to investigate latent processes underlying WCST performance in adolescents with OCD using computational modelling. As a proportion of the clinical sample were receiving serotonergic treatment, I also assessed how performance differed by medication status. It was hypothesised that the clinical sample would differ on model parameters representing feedback learning and rule exploration on this task, which are constructs of particular interest in this thesis.

2.2 Methods

2.2.1 Sample

Sixty-nine participants in total completed the WCST. All twenty-three patient participants formed the OCD group and 46 participants were in the CTL group. I stopped recruiting control participants for this task after the 46th control to prevent group sizes from being too different between OCD and CTL groups. Eleven OCD patients were receiving SSRI treatment at the time of the study while 12 were medication-naïve. Eight OCD patients were medicated with sertraline and 4 were medicated with fluoxetine. Mean SSRI dosage was 97.27mg (std dev: 58.33mg) and the dose range was 20 – 200 mg. IQ data was missing from one participant from the OCD group. Further demographic details are outlined in the Results section of this chapter.

2.2.2 Wisconsin Card Sorting Task

The WCST used in this study was run on a laptop via the Psychology Experiment Building Language programme (Mueller & Piper, 2014). The WCST contains up to 128 trials. Participants were shown 4 decks with a different combination of colours, numbers, and shapes (see Figure 2.1). They were instructed to sort cards appearing at the bottom of the screen, using a computer mouse,

according to one of three rules at a time, either number, colour or shape. The rule must be discovered using trial and error via visual feedback received after each card is sorted. Cards were sorted by clicking on the chosen deck using the laptop mousepad. If a card is sorted correctly, the feedback shown would be 'Correct'. If the card was sorted incorrectly, the feedback shown would be 'Incorrect' (see Figure 2.2 for stimulus presentation within the task). There was no time limit for a card to be sorted on each trial, but participants were told to answer as quickly and as accurately as possible.

After 10 cards have been successfully sorted consecutively, one set is completed and the sorting rule changes. The process continues until the participant either sorts all 128 cards or they complete 9 sets. The total time taken to complete the task is 10 minutes.

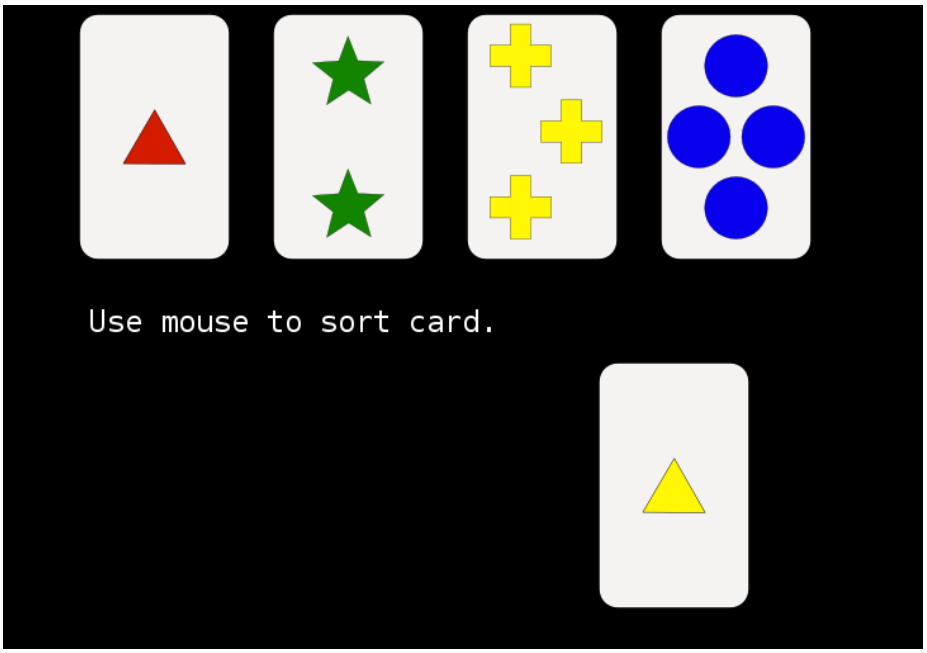

FIGURE 2.2: PRESENTATION OF THE WISCONSIN CARD SORTING TEST. THE FOUR STIMULUS CARDS ARE SHOWN AT THE TOP OF THE SCREEN. THE CARD TO BE SORTED IS SHOWN IN EACH TRIAL AT THE BOTTOM OF THE SCREEN.

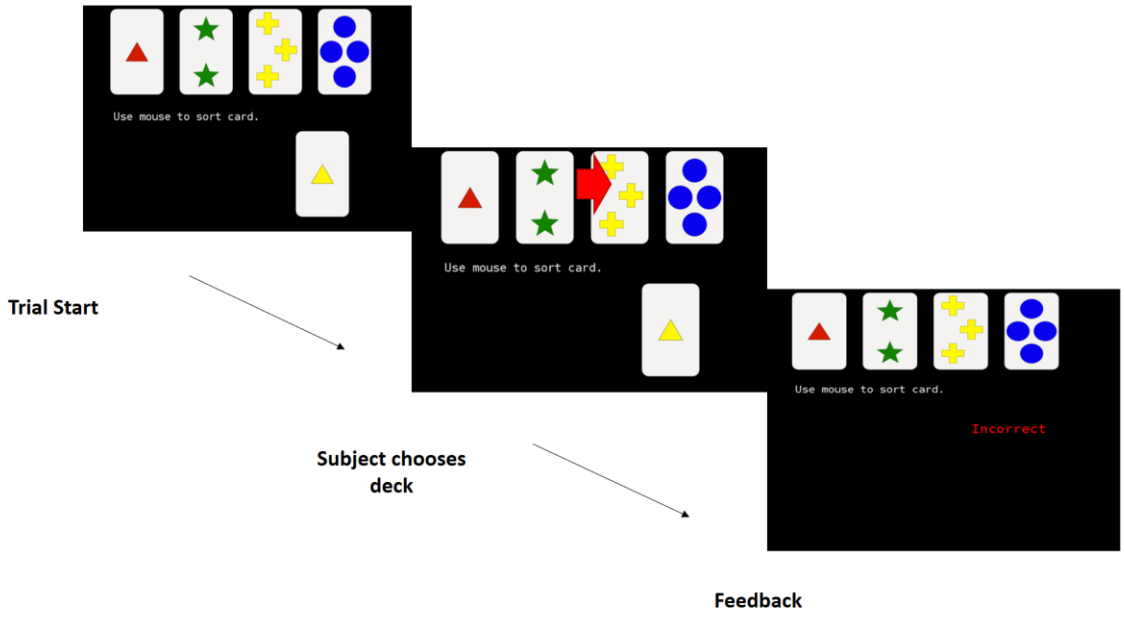

FIGURE 2.3: STIMULI PRESENTATION OF WISCONSIN CARD SORTING TASK

2.3 Statistical Analyses

2.3.1 Standard analyses

An a priori power analysis was conducted with $\alpha = .05$ (two-tailed), power (1-β) set to .8, and mean and standard deviation based on statistically significant differences in WCST performance between paediatric OCD patients and healthy participants from Shin et al.'s (2008) study. The analysis called for 62 subjects in each group, indicating that my current study is underpowered. However, the sample size I have employed is considerably larger than a proportion of past studies that have shown a significant WCST impairment in paediatric OCD patients (Isik Taner et al., 2011; M. S. Shin et al., 2008), but it is smaller than the sample of paediatric patients employed in Baykal et al. (2014).

All statistical analyses of measures from the WCST were implemented in RStudio 3.5.0.

The following outcome measures were analysed: number of sets completed (out of 9), percentage perseverative errors (incorrectly choosing a deck based on the rule from the previous set), percentage of non-perseverative errors (other errors that are not perseverative), percentage of unique errors (when a deck is chosen that does not match the test card on any rule), number of set

maintenance failures (number of times participants chose the wrong deck when completing the sets), number of trials needed to complete first set, and response times in milliseconds (ms). These are measures commonly analysed in studies utilising the WCST (Andrés et al., 2008; D. A. Geller et al., 2018; Gläscher et al., 2019; Isik Taner et al., 2011; Somsen, 2007; Somsen, Van Der Molen, Jennings, & Van Beek, 2000).

To assess the effect of Group (CTL vs OCD) on each outcome measure, multivariate linear regressions were conducted. Aside from the Group variable, the following confounding variables were added into the regression models to control for their effects 1) Z-score standardised ages as WCST performance has been found to be age-dependent (Somsen, 2007; Somsen et al., 2000), 2) intelligence scores measured using the WASI-II as IQ was found to correlate with WCST performance (Foley, Garcia, Shaw, & Golden, 2009) and studies have reported that children with OCD show inferior performance on non-verbal IQ assessments compared to typically developing children (Abramovitch, Anholt, Raveh-Gottfried, Hamo, & Abramowitz, 2018; Batistuzzo et al., 2020), and lastly 3) gender as gender differences are common when assessing general cognitive test performance (De Luca et al., 2003; Gur et al., 1999).

Homoscedascity of residuals obtained from each regression model were assessed using the Breusch-Pagan test. When the assumption of homoscedascity of residuals was violated, a sandwich variance estimate function from the ‘sandwich’ R package (Zeileis, 2004) was applied to the regression model(s). This enabled the extraction of standard errors that were robust to non-constant variance. P-values were calculated using these new standard errors.

Next, significance levels for the regression analyses were adjusted according to the Benjamini-Hochberg (BH) procedure to control the false detection rate arising from multiple comparisons using the ‘p.adjust’ function in base R.

The regression analyses were then repeated, this time exploring the effects of medication on the outcome measures. The patient group was divided into MED- and MED+. Post-hoc comparisons between the 3 independent groups were conducted using the Tukey test with Bonferroni correction.

All statistical tests reported are two-tailed.

Lastly, Pearson correlations were conducted to decipher the relationships between task measures and clinical measures.

2.3.2 Computational Model

The main model used in this study is identical to the one used by Gläscher et al. (2019) and was originally described by Bishara et al. (2010). It has 4 free parameters to be estimated from fitting the model to data, namely reward rate (*r*, how quickly attention weights change to rewarding feedback), punishment rate (*p*, how quickly attention weights change to punishing feedback), decision consistency (*d*, how much deck choice is influenced by attention weights), attentional focusing (*f*, only important on trials with ambiguous feedback and represents the degree to which the update is focused only on the category/rule with the largest attention weight).

The dependent variables fed into the model are an outcome variable which represent whether a trial was rewarded or not (1 or 0) and a matching matrix which quantify which categories (colour, number, or shape) associated with a chosen deck match the test card. For instance, if the chosen deck matched the test card based on colour only, the matching matrix for that trial would be defined as

$$m = \begin{bmatrix} 1 \\ 0 \\ 0 \end{bmatrix} \text{ – Equation 2.1}$$

The model calculates the probabilities associated with choosing each deck as a function of attention weights (a), which represents the weight given to each category per trial. The matrix elements of the attention signal always sum to one. It was assumed that for each participant's first trial, the attention weights are divided evenly between categories:

$$a = \begin{bmatrix} .333.. \\ .333.. \\ .333.. \end{bmatrix} \text{ – Equation 2.2}$$

Attention weights are updated using a feedback signal (s), which represents whether the categories were rewarded or not. For example, in the case where a chosen deck matches the test card based on only colour and nothing else, and the trial is rewarded, the feedback signal would look like this,

$$s = \begin{bmatrix} 1 \\ 0 \\ 0 \end{bmatrix} \text{ – Equation 2.3}$$

with each element of s representing colour, number, and shape respectively. The current attention weights are updated based on the feedback signal using the following equations:

$\mathbf{a}_{t+1} | \text{rewarded}_t = (1-r)a_t + r\mathbf{s}$ - if trial was rewarded – Equation 2.4

$\mathbf{a}_{t+1}|\text{punished}_t = (1\text{-}p)a_t + p\mathbf{s}$ - if trial was punished – Equation 2.5

where t refers to the current trial. Parameters *r* and *p* determine how rapidly attention weights change toward feedback signals following rewarding and punishing feedback respectively.

In the example above, the feedback is unambiguous as the chosen deck matches the test card on only category. However, in some cases where more than one category is matched (for example, both colour and shape), the feedback signal relies on the free parameter *f* to modulate how focused or wide the attention is on each category's feedback. When *f* approaches 0, attention is split evenly between the matching categories:

$$s = \begin{bmatrix} 0.5 \\ 0.5 \\ 0 \end{bmatrix}$$ – Equation 2.6

As *f* increases, the feedback signal is split proportionally to current attention weights. For example, if the attention weight for colour is higher than shape, the feedback signal would follow suit and perhaps be represented by:

$$s = \begin{bmatrix} 0.75 \\ 0.25 \\ 0 \end{bmatrix}$$ – Equation 2.7

The following equations represent how the feedback signal is modulated by the attention weights and matching matrix.

$s_t|\text{reward} = \frac{\mathbf{m_t}\mathbf{a}_t^f}{\sum \mathbf{m_t}\mathbf{a}_t^f}$ – Equation 2.8

$s_t|\text{punish} = \frac{(1-\mathbf{m_t})\mathbf{a}_t^f}{\sum (1-\mathbf{m_t})\mathbf{a}_t^f}$ – Equation 2.9

When outcome on the current trial is correct, the feedback signal is computed only with the matching attention weights, and when the outcome is incorrect, only the non-matching attention weights contribute to the feedback signal.

Finally, the probability of choosing a specific deck is defined as

$P = \frac{\mathbf{m}_t' \boldsymbol{a}_t^d}{\sum \boldsymbol{a}_t^d}$ – Equation 2.10

where the *d* parameter influences the predicted probability of choosing a deck per trial. As *d* becomes higher, choices become more random and less dependent on attention weights (more exploratory). As *d* becomes lower, choices are heavily constrained by attention weights (more exploitative). $\mathbf{m}_t'$ is simply the matching matrix, $\mathbf{m}_t$,transposed to enable matrix multiplication (dot product) with $\boldsymbol{a}_t$.

The full model described above with 4 free parameters was compared to 4 other degenerate models. Each degenerate model had one parameter fixed to assess the contribution of each parameter to capturing behaviour on the task.

The 1st two alternative models (RPD1 and RPD0) fixed the *f* parameter to be 1 and 0 respectively. The 3rd alternative model (RP1F) fixed *d* to be 1, and the final model (RRDF) assumed a single common learning rate for both reward and punishment.

Models were fit to trial-by trial behavioural data using hierarchical Bayesian estimation by estimating the posterior distribution (distribution of data after model fitting) of the model parameters at the individual subject- and group- levels. At the group level, Uniform (0,1) distributions were used as priors (predictions about the distribution of the data before model-fitting) for the *r* and *p* parameters, while Uniform (0,5) distributions were used for *d* and *f* parameters. Inter-subject variance for *r* and *p* were sampled from Half-normal (0,0.05) distributions, while inter-subject variance for *d* and *f* were sampled from Half-normal (0,1) distributions. Individual subject parameters were represented by a Gaussian prior distribution, and the mean and variance of the prior distributions were sampled from the group-level and inter-subject variability distributions.

Modelling data hierarchically reduces the influence of artefacts on model fitting and parameter estimation. Regularising individual parameters in this way produces better individual estimates and enables reliable group-level tests (Piray, Dezfouli, Heskes, Frank, & Daw, 2019). Furthermore, the shrinkage of estimates drawn from a higher level distribution leads to more conservative estimates, leading to an automatic multiple comparisons correction without a reduction in power which is often seen in classical statistics (Gelman, Hill, & Yajima, 2012; Gelman & Tuerlinckx, 2000; Kruschke, 2011).

Computation of the posteriors were conducted using Markov Chain Monte Carlo (MCMC) sampling using JAGS software (Plummer, 2003). Four randomly initialised MCMC chains were run during model-fitting. Model comparison was conducted by calculating the Deviance Information Criterion (DIC) which takes into account accuracy of model fit and penalises model complexity (number of free parameters). Lower DIC values indicate better fit.

Posterior distributions of parameters were interpreted using the 95% highest posterior density interval (HDI), also known as the Bayesian credible interval. All values within the interval have a higher probability density (i.e. higher credibility) than any value outside the HDI. Parameter comparisons between OCD and CTL were calculated by subtracting the posterior distributions of the CTL group-parameters from the posterior distributions of the OCD group-parameters, generating the group mean differences per parameter. The 95% HDIs of the posterior distribution for the group mean differences were calculated and inspected to check whether they reliably included zero (indicating no difference between groups).

Lastly, model-fitting was repeated to explore the effects of medication on behaviour. Group differences between CTL, MED-, and MED+ were analysed.

Parameter recovery and simulation (which involves simulating data from the model using parameter values obtained from fitting the model to real data, and in turn fitting the model to the simulated data to check if parameter values can be recovered) was not run here as the winning model had already been fully validated in the study by Gläscher et al. (2019). Parameter recovery is described in more detail in Chapters 4 and 6.

2.4 Results

2.4.1 Standard Analyses (CTL vs OCD)

Table 2.1 summarises the demographic and clinical characteristics for both groups. Groups were matched for gender, age, and IQ (intelligence quotient) scores. However, OCD had significantly elevated depression, anxiety, and obsessive-compulsive severity scores compared to CTL.

Table 2.1: Mean scores and standard deviations per group and statistical tests.

	CTL (n = 46)	**OCD (n = 23)**	**STATISTIC**
GENDER(F:M)	28/18	14/9	$\chi 2$ (1)=0, p = 1
AGE	16.59 ± 1.78	15.95 ± 1.67	t(67) = 1.44; p = .15
WASI-II (IQ)[a]	107.61 ± 11.62	108.32 ± 13.80	t(66) = -0.22; p = .83
BDI **	46.46 ± 5.27	58.35 ± 8.95	t(29.84) = -5.88; p = 2.96e-06
BAI **	45.98 ± 7.66	66.30 ± 9.55	Z = -6.52; p = 6.846e-11
OCI **	8.13 ± 6.49	30.74 ± 14.08	Z = -5.93; p = 2.99e-09
CY-BOCS	N/A	23.45 ± 5.19	N/A

Key: CTL: Control Group; OCD: Obsessive-Compulsive Disorder group; WASI-II: Wecshler's Abbreviated Scale of Intelligence – II; IQ: Intelligence Quotient; BDI: Beck's Depression Inventory (t-scored); BAI: Beck's

Anxiety Inventory (t-scored); OCI: Obsessive-Compulsive Inventory; CY-BOCS: Child Yale-Brown Obsessive-Compulsive Scale. *p<.05; **p<.01, [a]missing data from one OCD participant.

Table 2.2 displays the main group results per dependent measure as well as the results from the regression analyses.

Table 2.2: Regression results of Wisconsin Card Sorting Task data.

Dependent Variable	CTL (M ± SD)	OCD (M ± SD)	Independent Variable	Coefficient Estimate	Fixed Effect (t-value)	se	df	BH adjusted p-values	Adjusted R^2	Test Used
Number of sets completed	7.95 ± 1.48	7.61 ± 2.13	Group	-0.3478	-0.79	0.44	67	.50	0.0055	Linear Regression
p(Perseverative errors)	0.12 ± 0.028	0.13 ± 0.07	Group	0.0060	Z = 0.41	0.015	N/A	.68	0.011	Linear Regression with Sandwich Estimator
p(Non perseverative errors)	0.058 ± 0.040	0.077 ± 0.068	Group	0.018	1.41	0.013	67	.28	0.014	Linear Regression
Mean RT	1420.49 ± 279.71	1611.96 ± 313.01	**Group**	191.47	2.58	74.33	67	**.043**	0.077	Linear Regression
Failure to maintain set	0.93 ± 1.06	1.34 ± 1.56	Group	0.41	1.30	0.32	67	.28	0.010	Linear Regression
Number of trials needed to complete first set	14.80 ± 9.58	18.96 ± 16.67	Group	4.15	1.32	3.16	67	.28	0.011	Linear Regression
p(Unique Errors)	0.0014 ± 0.0045	0.0055 ± 0.080	**Group**	0.0042	2.78	0.0015	67	**.043**	0.090	Linear Regression

Note: Linear regression with sandwich estimator outputs a Z-value instead of a t-value. Independent measures in **bold** font indicate significance at p<.05. Key- CTL: Control group; OCD: Patient group; M: mean; SD: standard deviation; df: degrees of freedom; BH: Benjamini-Hochberg Correction; CI: confidence interval; SE: regression standard error; p(): proportion; R2: r-squared, measure of effect size.

The regression analyses revealed that OCD had showed slower response times (Coefficient estimate = 191.47, $t(67) = 2.58$, $p = .043$) and an increased proportion of unique errors compared to CTL (Coefficient estimate = 0.0042, $t(67) = 2.78$, $p = .043$).

The analyses were repeated including age, IQ, and gender as covariates (see Table 2.3 and Figure 2.3).

Table 2.3: Regression results from Wisconsin Card Sorting Task data controlling for age, gender, and IQ.

DV	Independent Variable	Coefficient Estimate	Fixed Effect (t-value)	df	se	BH adjusted p-values	Adjusted R^2	Test Used
Number of sets completed	Group	-0.14	-0.33	63	0.41	.74	0.19	Linear Regression
	Gender	-0.71	-1.79		0.40	.55		
	Age	0.66	3.37		0.20	**.0045**		
	IQ	0.032	2.02		0.016	.11		
p(Perseverative errors)	Group	0.44	Z = 0.36	N/A	1.21	.74	0.18	Linear Regression with Sandwich Estimator
	Gender	0.96	Z = 1.00		0.96	.57		
	Age	-1.40	Z = -2.42		0.58	.032		
	IQ	-0.14	Z = -3.30		0.044	**.0069**		
p(Non perseverative errors)	Group	1.39	1.05	63	1.32	.44	0.058	Linear Regression
	Gender	0.87	0.68		1.28	.61		
	Age	-1.36	-2.20		0.63	**.040**		
	IQ	0.047	-0.92		0.051	.50		
Mean RT	Group	150.96	2.28	63	66.29	.092	0.32	Linear Regression
	Gender	41.72	0.65		64.41	.61		
	Age	-139.34	-4.42		31.53	**.00028**		
	IQ	-7.03	-2.74		2.57	**.028**		
Failure to maintain set	Group	0.35	1.12	63	0.31	.44	0.11	Linear Regression
	Gender	0.43	1.41		0.30	.57		
	Age	-0.36	-2.42		0.15	**.032**		
	IQ	-0.017	-1.44		0.012	.27		
Number of trials needed to complete first set	Group	3.30	1.01	63	3.23	.44	0.039	Linear Regression
	Gender	-1.26	-0.40		3.14	.69		
	Age	-3.32	-2.17		1.54	**.040**		
	IQ	-0.060	-0.48		0.13	.74		
p(Unique Errors)	Group	0.38	Z = 2.29	N/A	0.17	.092	0.15	Linear Regression with Sandwich Estimator
	Gender	-0.14	Z = -0.98		0.14	.57		
	Age	-0.18	Z = -1.74		0.10	.082		
	IQ	-0.0012	Z = -0.24		0.0050	.81		

Note: Linear regression with sandwich estimator outputs a Z-value instead of a t-value. Independent measures in **bold** font indicate significance at $p<.05$. M: mean; SD: standard deviation; df: degrees of freedom; BH: Benjamini-Hochberg Correction; CI: confidence interval; SE: regression standard error; IQ: intelligence scores; p(): proportion, R2: r-squared, measure of effect size.

When controlling for the aforementioned variables, Group (OCD vs CTL) was no longer a significant predictor of response times and proportion of unique errors ($p > .05$). Age emerged as a significant predictor for several dependent variables: older participants completed more sets (Coefficient estimate = 0.66, $t(63) = 3.37$, $p = .0045$), committed less non-perseverative errors (Coefficient estimate = -1.36, $t(63) = -2.20$, $p = .040$), had faster response times (Coefficient estimate = -139.34, $t(63) = -4.42$, $p = .00028$), maintained sets more (Coefficient estimate = -0.36, $t(63) = -2.42$, $p = .032$), and required less trials to complete the first category (Coefficient estimate = -3.32, $t(63) = -2.17$, $p = .040$). Additionally, the analyses revealed that those with higher IQ committed less perseverative errors (Coefficient estimate = -0.14, $Z = -3.30$, $p = .0069$) and had faster response times (Coefficient estimate = -7.03, $t(63) = -2.74$, $p = .028$).

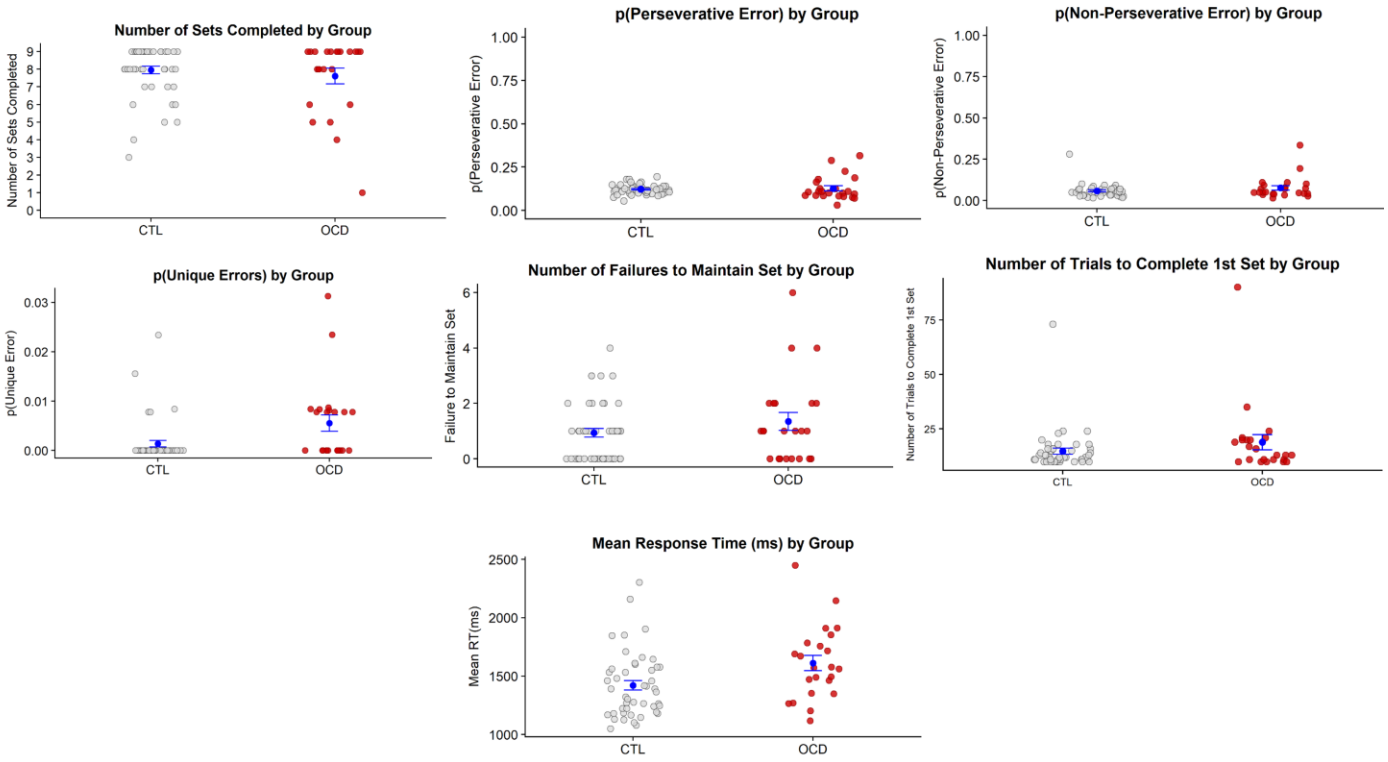

FIGURE 2.4: PLOTS COMPARING CTL VS OCD ON 7 OUTCOME MEASURES FROM THE WISCONSIN CARD SORTING TEST. AT FIRST, OCD APPEARED TO SHOW SIGNIFICANTLY MORE UNIQUE ERRORS AND SLOWER RESPONSE TIMES COMPARED TO CTL. HOWEVER, THESE DIFFERENCES CEASED TO BE SIGNIFICANT AT P<.05 WHEN CONTROLLING FOR AGE, GENDER, AND IQ.

2.4.3 Exploratory Medication Analyses

The analyses above were repeated this time dividing the OCD group into those not receiving (MED-) and receiving (MED+) SSRI medication. The following results are termed ‘exploratory’ as there are too few participants in each group to draw strong conclusions. Demographic, intelligence, and clinical scores are found in Table 2.4. No apparent differences were found between groups on measures of age, IQ, and gender composition. MED- and MED+ displayed increased anxiety, depression, and obsessive-compulsive scores compared to CTL.

Table 2.4: Mean scores and standard deviations per group and statistical test.

	CTL (n = 46)	**MED- (n = 12)**	**MED+ (n = 11)**	**STATISTIC**	**PAIRWISE COMPARISONS**
GENDER(F:M)	28/18	8/4	6/5	$\chi 2$ (2)=0.35 , p = 0.84	-
AGE	16.59 ± 1.78	15.87 ± 1.60	16.04 ± 1.81	$\chi 2$ (2)=4.50 , p = 0.11	-
WASI-II (IQ)[a]	107.61 ± 11.62	109.82 ± 12.99	106.82 ±15.03	F(2,65) = 0.19, p=0.83	-
BDI **	46.46 ± 5.27	56.67 ± 9.52	60.18 ± 8.33	F(2,66) = 42.1, p=1.64e-12	CTL < MED- & MED+ MED- = MED+
BAI **	45.98 ± 7.66	66.08 ± 9.53	66.55 ± 10.03	$\chi 2$ (2)=42.57 , p = 5.7e-10	CTL < MED- & MED+ MED- = MED+
OCI **	8.13 ± 6.49	32.33 ± 14.74	29.00 ± 13.82	$\chi 2$ (2)=35.30 , p = 2.16e-08	CTL < MED- & MED+ MED- = MED+
CY-BOCS	N/A	24.73 ± 5.88	22.18 ± 4.29	t(20) = 1.16; p=0.26	N/A

Key: CTL: Control Group; MED-: Unmedicated patient group; MED+: Medicated patient group; WASI-II: Wecshler's Abbreviated Scale of Intelligence – II; IQ: Intelligence Quotient; BDI: Beck's Depression Inventory (t-scored); BAI: Beck's Anxiety Inventory (t-scored); OCI: Obsessive-Compulsive Inventory; CY-BOCS: Child Yale-Brown Obsessive-Compulsive Scale. *p<.05; **p<.01; [a] missing data from one MED- participant.

Post-hoc tests revealed that compared to CTL, MED+ and MED- groups had elevated depression (Pairwise t-tests, MED- vs CTL: t(66) = 4.72; p = 3.80e-05, MED+ vs CTL: t(66) = 6.13; p = 1.66e-06), anxiety (Dunn's test, MED- vs CTL: p = 5.60e-07, MED+ vs CTL: p = 2.25e-06), and obsessive-compulsive scores (Dunn's tests, MED- vs CTL: p = 3.18e-06, MED+ vs CTL: p = 5.23e-05). There were no differences on these measures between MED- and MED+ (all p > .05).

Per-group results and results of the regression analyses investigating effects of medication status on the WCST dependent variables are included in Tables 2.5 and 2.6. MED+ had a significant effect on response times (Coefficient estimate = 320.25, t(62) = 3.36, p = .0091), and a marginally significant effect on proportion of unique errors (Coefficient estimate = 0.0073, Z =2.43 , p = .052).

Table 2.5: Summary of Wisconsin Card Sorting Test scores per group and per dependent variable

	CTL (n=46) (M ± SD)	MED- (n=12) (M ± SD)	MED+ (n=11) (M ± SD)
Number of sets completed	7.96 ± 1.48	8.17 ± 1.34	7.00 ± 2.68
p(Perseverative errors)	0.12 ± 0.028	0.13 ± 0.083	0.12 ± 0.056
p(Non-perseverative errors)	0.058 ± 0.040	0.063 ± 0.046	0.091 ± 0.087
p(Unique errors)	0.0014 ± 0.0045	0.0027 ± 0.0040	0.0087 ± 0.010
Mean RT	1420.49 ± 279.71	1493.91 ± 230.50	1740.75 ± 349.49
Failure to maintain set	0.93 ± 1.06	0.83 ± 0.83	1.91 ± 1.97
Number of trials needed to complete first set	14.80 ± 9.58	16.83 ± 7.31	21.27 ± 23.27

Key: CTL: Control Group; MED-: Unmedicated patient group; MED+: Medicated patient group; p(): proportion.

Table 2.6: Regression results looking at effects of medication status on dependent measures of Wisconsin Card Sorting Test.

Dependent Variable	**Independent Variable**	**Estimate**	**Fixed Effect (t-value)**	**se**	**df**	**BH adjusted p-value**	**Adjusted R^2**	**Test Used**
Number of sets completed	MED- MED+	0.21 -0.96	Z =0.49 Z= -1.19	0.43 0.80	N/A	.75 .27	0.020	Linear Regression with Sandwich Estimator
p(Perseverative errors)	MED- MED+	0.012 -0.00060	Z= 0.52 Z= -0.037	0.023 0.017	N/A	.75 .97	0.020	Linear Regression with Sandwich Estimator
p(Non-perseverative errors)	MED- MED+	0.0052 0.033	0.32 1.93	0.016 0.017	62	.75 .14	0.024	Linear Regression
Mean RT	MED- **MED+**	73.42 320.25	0.80 3.36	92.09 95.35	62	.75 **.0091**	0.12	Linear Regression
Failure to maintain set	MED- MED+	-0.10 0.97	Z= -0.37 Z= 1.66	0.278 0.59	N/A	.75 .17	0.0059	Linear Regression with Sandwich Estimator
Number of trials needed to complete first set	MED- MED+	2.03 6.47	0.51 1.56	4.02 4.16	62	.75 .18	0.0067	Linear Regression
p(Unique errors)	MED- MED+	0.0013 0.0073	Z= 1.03 Z= 2.43	0.0013 0.0030	N/A	.75 .052	0.00096	Linear Regression with Sandwich Estimator

Note: Some dependent variables have a Z value reported as a fixed effect value as the linear regression with sandwich estimator outputs a Z-value instead of a t-value. Independent measures in bold font indicate significance at $p<.05$. Key: MED-: Unmedicated patient group; MED+: Medicated patient group; M: mean; SD: standard deviation; df: degrees of freedom; BH: Benjamini-Hochberg Correction; CI: confidence interval; SE: regression standard error; IQ: intelligence scores; p(): proportion.

When controlling for age, IQ, and gender (see Table 2.7), MED+ became a significant predictor for proportion of unique errors (Coefficient estimate = 0.68, $Z = 2.60$, $p = .033$) alongside predicting slower response times (Coefficient estimate = 268.28, $t(62) = -3.25$, $p = .013$).

Table 2.7: Regression results looking at effects of medication status on dependent measures of Wisconsin Card Sorting Test, controlling for age, gender, and IQ.

Dependent Variable	Independent Variable	Estimate	Fixed Effect (t-value)	df	se	BH adjusted p-value	Adjusted R^2	Test Used
Number of sets completed	MED-	0.42	0.80	62	0.522	.94	0.21	Linear regression
	MED+	-0.68	-1.31		0.52	.23		
	Gender	-0.66	-1.69		0.39	.46		
	Age	0.67	3.47		0.19	**.0033**		
	IQ	0.030	1.91		0.016	.14		
p(Perseverative errors)	MED-	1.57	Z=0.76	N/A	2.072	.94	0.19	Linear regression with Sandwich Estimator
	MED+	-0.68	Z=-0.55		1.23	.58		
	Gender	1.06	Z=1.11		0.95	.46		
	Age	-1.38	Z=-2.46		0.560	**.024**		
	IQ	-0.148	Z=-3.27		0.045	**.0074**		
p(Non-perseverative errors)	MED-	-0.010	-0.006	62	1.70	1.00	0.068	Linear regression
	MED+	2.76	1.64		1.69	.19		
	Gender	0.75	0.59		1.28	.65		
	Age	-1.39	-2.22		0.62	**.038**		
	IQ	-0.042	-0.82		0.051	.58		
Mean RT	MED-	31.72	0.38	62	83.11	.94	0.36	Linear regression
	MED+	268.28	3.25		82.57	**.013**		
	Gender	31.50	0.50		62.5	.65		
	Age	-141.58	-4.63		30.56	**.00013**		
	IQ	-6.58	-2.64		2.50	**.037**		
Failure to maintain set	MED-	-0.13	-0.34	62	0.39	.94	0.15	Linear regression
	MED+	0.82	2.10		0.39	.094		
	Gender	0.39	1.30		0.30	.46		
	Age	-0.37	-2.54		0.15	**.024**		
	IQ	-0.016	-1.32		0.011	.34		
Number of trials needed to complete first set	MED-	1.05	0.25	62	4.19	.94	0.035	Linear regression
	MED+	5.45	1.31		4.16	.23		
	Gender	-1.45	-0.46		3.15	.65		
	Age	-3.37	-2.19		1.54	**.038**		
	IQ	-0.052	-0.41		0.13	.79		
p(Unique errors)	MED-	0.073	Z=0.48	N/A	0.15	.94	0.22	Linear regression with Sandwich Estimator
	MED+	0.68	Z=2.60		0.26	**.033**		
	Gender	-0.17	Z=-1.21		0.14	.46		
	Age	0.19	Z=-1.94		0.096	.052		
	IQ	-0.000051	Z=-0.010		0.0050	.99		

Note: Linear regression with sandwich estimator outputs a Z-value instead of a t-value. Independent measures in bold font indicate significance at $p<.05$. Key: MED-: Unmedicated patient group; MED+: Medicated patient group; M: mean; SD: standard deviation; df: degrees of freedom; BH: Benjamini-Hochberg Correction; CI: confidence interval; SE: regression standard error; IQ: intelligence scores; p(): proportion.

Post-hoc Tukey comparisons with Bonferroni correction revealed that MED+ had slower/increased response times compared to CTL (p = .0051). There were no significant differences in response time between MED- and MED+ (p = .067) as well as between MED- and CTL (p = .92). Post-hoc Tukey comparisons were also conducted for proportion unique errors as MED+ emerged as a significant predictor after controlling for confounding variables. It was revealed that MED+ committed more unique errors compared to CTL (p =.0014) and MED- (p =.031). There were no significant differences on this measure between CTL and MED- (p =.92). See Figure 2.4 for visualisation of these group differences.

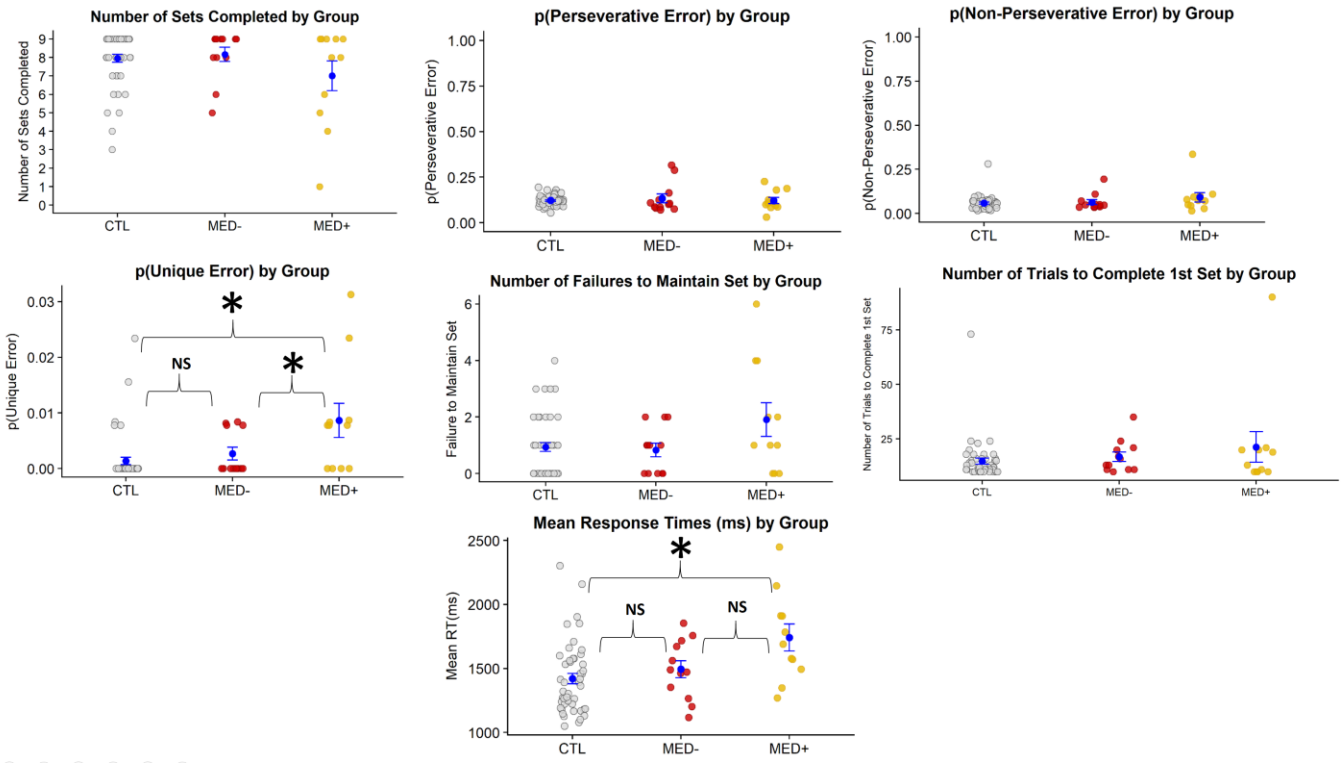

FIGURE 2.5: PLOTS COMPARING CTL VS MED- VS MED+ ON 7 OUTCOME MEASURES FROM THE WISCONSIN CARD SORTING TEST. POST-HOC PAIRWISE TUKEY TESTS REVEALED THAT MED+ SHOWED MORE UNIQUE ERRORS COMPARED TO MED- AND CTL (WITH NO DIFFERENCES BETWEEN MED- AND CTL). ADDITIONALLY, MED+ HAD SLOWER RESPONSE TIMES COMPARED TO CTL (NO DIFFERENCES BETWEEN CTL AND MED-, AND BETWEEN MED- AND MED+). *-P<.05, N.S.-NON-SIGNIFICANT.

2.4.4 Modelling Results

The winning model from the computation modelling analyses revealed the RPDF model to be the winning model. Deviance Information Criteria (DIC) results are displayed in Table 2.8.

Table 2.8: Comparison of model performance

Model	Description	Number of parameters	DIC
RPDF	Full model	4	7204.973
RPD1	Attentional focusing (f) fixed at 1	3	7833.797
RPD0	Attentional focusing (f) fixed at 0	3	7364.194
RP1F	Decision consistency (d) fixed at 1	3	7285.828
RRDF	Identical learning rate for reward and punishment	3	7334.887

The lower the DIC the better the model-fit. Hence the full RPDF model was the winning model.

No group differences were found on any of the parameters when conducting group mean differences analyses (see Figure 2.5).

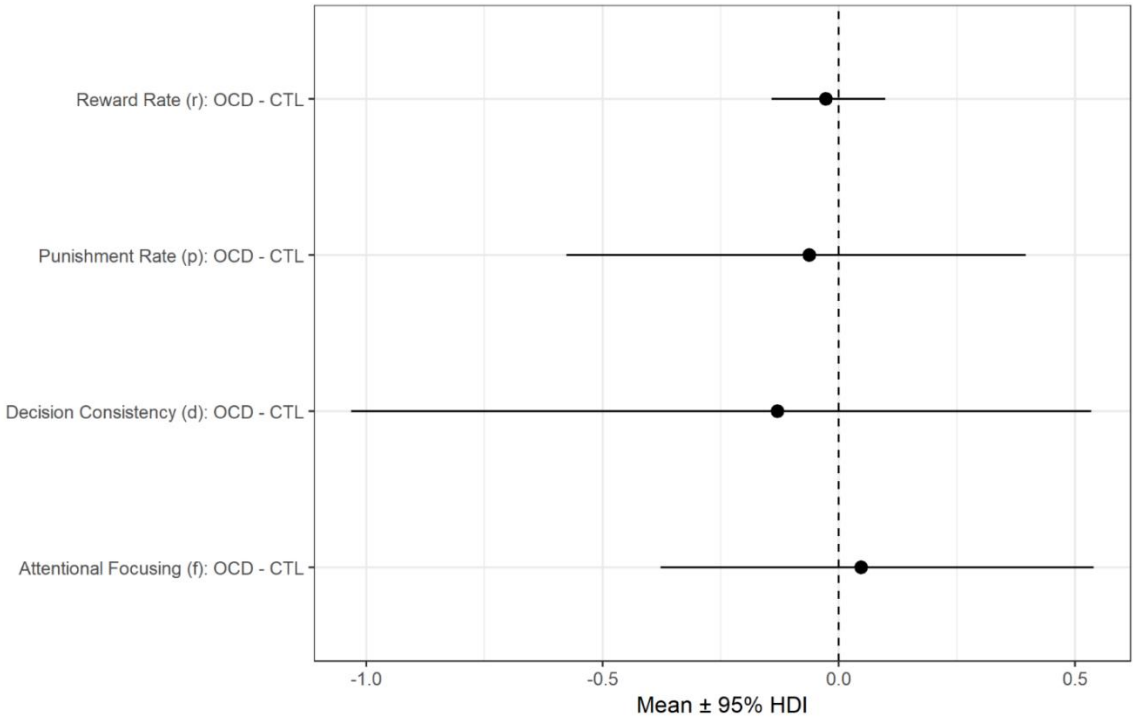

FIGURE 2.6: SUMMARY OF GROUP DIFFERENCES PER PARAMETER FROM THE BEST-FIT COMPUTATIONAL MODEL. ERROR BARS REPRESENT THE HIGHEST DENSITY INTERVALS (HDI) OF THE POSTERIOR DISTRIBUTIONS OF GROUP DIFFERENCES (OCD-CTL) IN GROUP MEAN PARAMETER VALUES. ALL GROUP DIFFERENCE HDIS INCLUDED 0 INDICATING NO NOTICEABLE DIFFERENCES BETWEEN GROUPS FOR EACH PARAMETER.

There were also no group differences between parameters when dividing OCD into MED- and MED+ (see Figure 2.6).

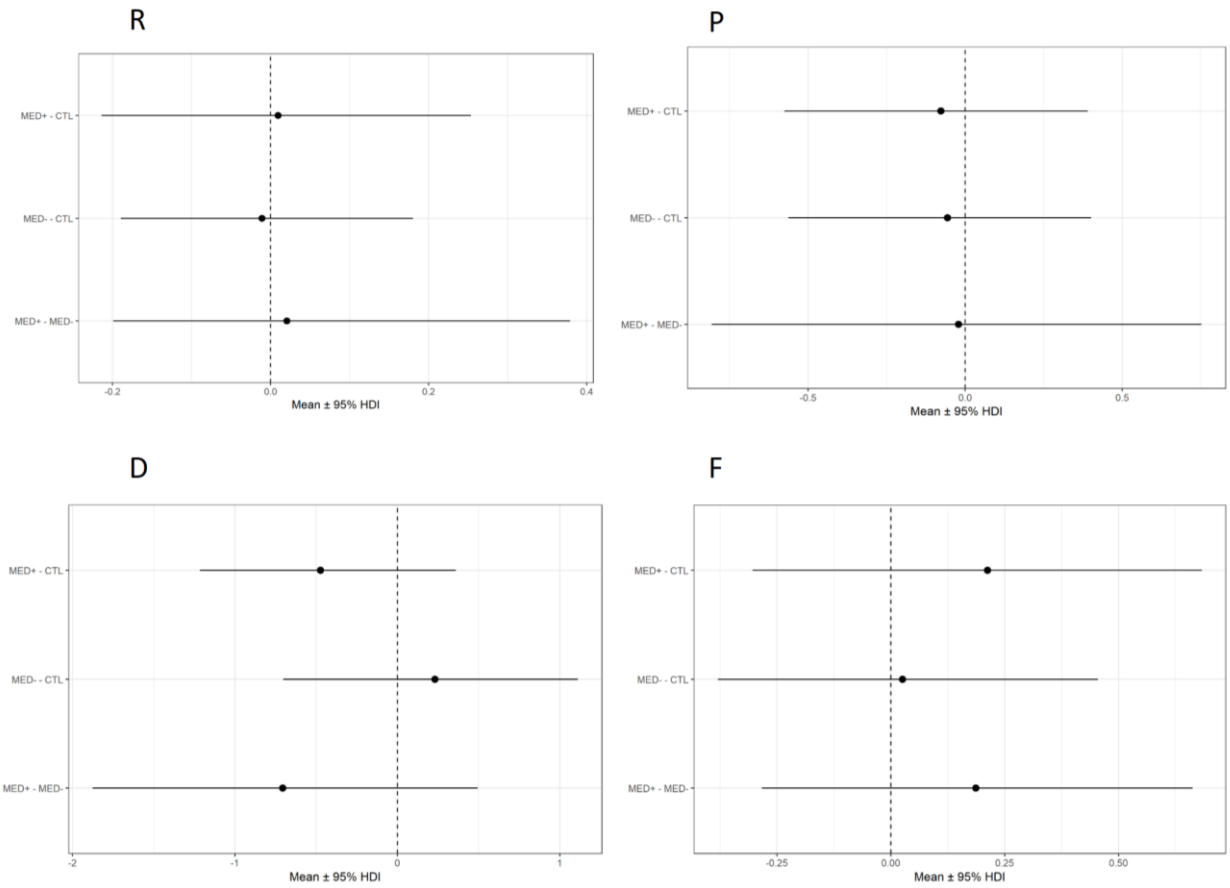

FIGURE 2.7: SUMMARY OF GROUP DIFFERENCES (CTL VS MED- VS MED+) PER PARAMETER FROM THE BEST-FIT COMPUTATIONAL MODEL. EACH PLOT REPRESENTS GROUP MEAN DIFFERENCE RESULTS FOR EACH MODEL PARAMETER: R – REWARD RATE, P- PUNISHMENT RATE, D – DECISION CONSISTENCY, F – ATTENTIONAL FOCUSING. ERROR BARS REPRESENT THE HIGHEST DENSITY INTERVALS (HDI) OF THE POSTERIOR DISTRIBUTIONS OF GROUP DIFFERENCES IN GROUP MEAN PARAMETER VALUES. ALL GROUP DIFFERENCE HDIS INCLUDED 0 INDICATING NO NOTICEABLE DIFFERENCES BETWEEN GROUPS FOR EACH PARAMETER.

2.4.5 Correlational Analyses

Correlations with obsessive-compulsive severity

When considering all participants, OCI and CY-BOCS scores were not predictive of any measures. Nevertheless, when conducting correlational analyses within groups, marked patterns seemed to emerge. Within OCD, higher OCI scores was unexpectedly associated with better performance on the task, wherein patients with higher OCI scores completed more sets (r =0.57, *p* =.0045), made less unique errors (r =-0.45, *p* =.030), and made less set maintenance failures (r =-0.42, *p* =.047). Additionally, patients with more severe OCD revealed higher punishment rates (r =0.55, *p* =.0061) and decision-consistency (r =0.42, *p* =.045). CY-BOCS scores also correlated with *p* parameter values (r =0.55, *p* =.0086). However, I suspected these relationships were confounded by age of participants, as age also correlated with task measures (see ‘Correlations with age and IQ’ section

below) as well as showed a relationship with OCI scores (r = 0.50; p = .014). Furthermore, there was a trend (although non-significant) for CY-BOCS scores to also correlate with age (r = 0.42; p = .054). Hence, I conducted a further partial Pearson's correlation to control for the effects and age, which indeed rendered the relationships between OCD severity and model parameter values insignificant in the OCD group (all p <.05).

The opposite effect was unveiled when considering only CTL: higher OCI scores were associated with decreased punishment rates (r =-0.34, p =.020) and decision-consistency (r =-0.30, p =.043) values. Incidentally, OCI scores within CTL were also associated with increased reward rates (r =0.34, p =.023). OCI scores did not correlate with age or IQ in these participants, suggesting possible confounding variables were not driving the relationships.

Within MED-, there appeared to be significant relationships between OCI/CY-BOCS scores and task measures, but these were no longer significant when controlling for age. Within MED+, no correlations between task/model measures and obsessive-compulsive severity emerged.

Correlations with anxiety and/or depression

When considering all participants, there was a significant negative relationship between depression scores and proportion of perseverative errors (r = -0.26, p = .031). When considering only MED-, more depressed participants made less non-perseverative errors (r=-0.36, p = .015).

Correlations with age and IQ

Within all participants, those with higher IQ scores made less perseverative errors (r = -0.33, p = .0060) and had higher p parameter values (r = 0.28, p = .021). Age showed a relationship with several dependent measures: older participants completed more sets (r =0.40, p = .00070), made less perseverative (r = -0.28, p = .018) and non-perseverative errors (r = -0.29, p = .016), had faster response times (r = -0.48, p = .000029), showed decreased set maintenance failures (r = -0.32, p = .0082), and had increased p (r =0.39, p = .0010) and d (r = 0.40, p = .00062) parameter values.

Within OCD, age continued to positively correlate with number of sets completed (r =0.43, p =.039), model p values (r =0.58, p =.036), and model d values (r =0.61, p =.028), while correlating negatively with proportion of perseverative errors (r =-0.50, p =.016). Moreover, higher IQ predicted less perseverative errors (r =-0.45, p =.037), faster response times (r =-0.60, p =.0032), lower r (r =-0.50, p =.018) and f (r =-0.38, p =.029) model values as well as higher p (r =0.52, p =.013) and d (r =0.47, p =.028) model values.

Next, within CTL only, older participants completed more sets (r=0.37, p =.011), made less non-perseverative (r=-0.36, p =.042) and unique errors (r=-0.26, p =.040), had faster response times (r=-0.48, p =.00066), made less set maintenance failures (r=-0.31, p = .033), and needed less trials to complete the first set (r=-0.37, p =.011). Additionally, older participants had increased d values (r= 0.34, p =.023).

Within MED-, participants with higher IQ had faster reaction times (r =-0.75; p =.0080).

Lastly, when considering only MED+, older participants and participants with higher IQ showed increased p (age: r =0.65, p =.031; IQ: r =0.77, p =.0058) and d (age: r =0.78, p =.0058; IQ: r =0.73, p =.010) parameter values.

Correlations with medication dosage

Increasing medication dosage was associated with higher IQ scores (r =0.61, p = .049), but did not significantly correlate with any task measures or model parameter values.

Correlations between task measures and model parameters

Lastly, to verify that model parameter values map onto standard WCST measures, further Pearson correlations between model parameter values (r,p,d,f) and standard task measures (number of sets completed, proportion perseverative errors, proportion non-perseverative errors, proportion unique errors, failure to maintain set, number of trials needed to complete first set, and mean response times) were conducted. These analyses were conducted first considering all participants, then separately with each group. The results of this are included in Table 2.9.

Table 2.9: Pearson correlation results between model parameters and standard task measures.

All Participants	**No. sets completed**	**p(perseverative errors)**	**p(non-perseverative errors)**	**p(unique errors)**	**Failure to maintain set**	**No. trials needed to complete 1st set**	**Mean RT**
r	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
p	r =0.75; *p* <.0001	r =-0.51; *p* <.0001	r =-0.55; *p* <.0001	n.s.	r =-0.52; *p* <.0001	r =-0.51; *p* <.0001	r =-0.33; *p* = .0064
d	r =0.70; *p* <.0001	n.s.	r =-0.51; *p* <.0001	n.s.	r =-0.51; *p* <.0001	r =-0.42; *p* = .0039	r = -0.24; *p* = .043
f	n.s.	r =0.25; *p* =.038	n.s.	n.s.	n.s.	n.s.	n.s.

OCD only	**No. sets completed**	**p(perseverative errors)**	**p(non-perseverative errors)**	**p(unique errors)**	**Failure to maintain set**	**No. trials needed to complete 1st set**	**Mean RT**
r	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
p	r = 0.81, *p* < .0001	r =-0.44 , *p* =.035	r =-0.54 , *p* =.0071	n.s.	r = -0.54, *p* = .0084	r = -0.45, *p* =.030	r =-0.54, *p* = .0084
d	r =0.72, *p* <.0001	n.s.	r = -0.56, *p* =.0050	n.s.	r = -0.51, *p* =.013	n.s.	r = -0.51, *p* = .014
f	n.s.	r = 0.55, *p* = .0063	n.s.	n.s.	n.s.	n.s.	r = 0.65, *p* = .00070

CTL only	**No. sets completed**	**p(perseverative errors)**	**p(non-perseverative errors)**	**p(unique errors)**	**Failure to maintain set**	**No. trials needed to complete 1st set**	**Mean RT**
r	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
p	r = 0.69, *p* <.0001	r = -0.68, *p* <.0001	r = -0.56, *p* <.0001	n.s.	r = -0.50, *p* = .00041	r =-0.60 , *p* <.0001	n.s.
d	r = 0.71, *p* <.0001	r = -0.59, *p* <.0001	r = -0.51, *p* = .00025	n.s.	r = -0.59, *p* < .0001	r = -0.50, *p* = .00039	n.s.
f	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.

MED- only	**No. sets completed**	**p(perseverative errors)**	**p(non-perseverative errors)**	**p(unique errors)**	**Failure to maintain set**	**No. trials needed to complete 1st set**	**Mean RT**
r	r = -0.73, *p* = .0073	n.s.	r = 0.77, *p* = .0032	r = 0.60, *p* = .040	n.s.	r = 0.76, *p* = .0042	n.s.
p	r = 0.82, *p* = .0018	n.s.	r = -0.77, *p* = .0036	n.s.	n.s.	r = -0.59, *p* = .043	n.s.

d	r =0.71 , *p* = .010	n.s.	r = -0.63, *p* = .027	n.s.	n.s.	n.s.	n.s.
f	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.

MED+ only	**No. sets completed**	**p(perseverative errors)**	**p(non-perseverative errors)**	**p(unique errors)**	**Failure to maintain set**	**No. trials needed to complete 1st set**	**Mean RT**
r	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
p	r = 0.83, *p* = .0014	n.s.	n.s.	n.s.	r =-0.79 , *p* =.0040	n.s.	n.s.
d	r = 0.79, *p* =.0039	n.s.	n.s.	n.s.	r = -0.74, *p* =.0086	n.s.	n.s.
f	n.s.	r =0.80 , *p* =.0029	n.s.	n.s.	n.s.	n.s.	r = 0.83, *p* = .0015

Key: R: reward rate, P: punishment rate, D: Decision Consistency, F: Attentional Focusing; CTL: Control group; OCD: Patient group; MED-: Unmedicated patient group; MED+: Medicated patient group; r: Pearson's Correlation Coefficient; n.s: not significant; p(): proportion; RT: response time.

2.4.6 Summary of Main Results

OCD and CTL showed overall comparable performance on all WCST measures when controlling for age, IQ and gender. However, MED+ committed significantly more unique errors than MED- and CTL, and also showed slower response times compared to CTL but not MED-. MED- was equivalent to CTL on all measures. There were no group differences on any of the computational model parameters considered.

2.5 Discussion

This is the first study that has aimed to fractionate cognitive processes contributing to WCST performance in adolescents with OCD using a computational model, originally conceptualised by Bishara et al. (2010). When assessing standard performance whilst controlling for age, gender, and intelligence, adolescents with OCD did not differ from healthy matched controls on any task measures. Group differences emerged when separating the OCD group by medication status: patients medicated with SSRIs exhibited more unique errors compared to control participants and non-medicated patients, and additionally displayed slower response times than controls. Next, contrary

to my hypothesis, computational modelling revealed no marked group differences on the parameters investigated. Nevertheless, I uncovered a few correlations between obsessive-compulsive traits and model parameter values within the control group that are discussed below.

2.5.1 Cognitive Flexibility

As described in the introduction of this chapter, the WCST is principally a test of cognitive flexibility. As adolescent patients in this study, regardless of medication status, did not differ from healthy controls on proportion of perseverative errors made, we can conclude the absence of a cognitive flexibility deficit in this sample. This is in line with previous paediatric OCD research that typically report no OCD-related impairment on the WCST (see Chapter 1). Additionally, this strengthens the notion that youths with OCD differ cognitively from adult patients, as the latter tend to show widespread deficits on this task (Fradkin et al., 2018). One line of reasoning for this is that cognitive flexibility becomes increasingly impacted as a function of disorder duration. Another explanation is that healthy adolescents perform less well on the task compared to adults due to their executive functions and frontal lobes still undergoing maturation. As a result, adolescents with OCD appear unimpaired when compared to healthy age-matched populations, but deficits in adulthood become more pronounced as patients are compared to adults with fully developed cognitive abilities. Nonetheless, research looking into age-dependent normative WCST scores has revealed that by the time healthy children are 10 years old, their performance on the task is indistinguishable from healthy adults (Chelune & Baer, 1986), suggesting the lack of group differences is not a developmental artefact. The cognitive differences between adults and adolescents with OCD is discussed further in the General Discussion (Chapter 7).

2.5.2 Medication Effects

In this study I uncovered an unexpected effect of medication; medicated patients appeared to make more random guesses on the task as demonstrated by their tendency to choose decks that did not fit any rule presented on the test card. As a caveat, the variance within the medicated group on this measure was high and hence these results should be interpreted with caution.

Unique errors are posited to indicate a lack of recognition or awareness of rules in the task. Such errors are usually made by very young children tested on this paradigm (Somsen, 2007), who may have difficulty attending to and recognising all the different rules. Hence, it could be that the medicated patients in my study have attentional and rule-learning impairments. A learning deficit, in particular, has been thought to be a feature of adolescent-OCD (Gottwald et al., 2018), but it is undetermined why the effect is most noticeably present in the medicated patients in this current study.

Furthermore, if attention and learning were compromised in this group, it is unusual that the deficit is specific to unique errors and does not extend to other task measures such as failures to maintain sets which is also thought to reflect attentional issues (Mullane & Corkum, 2007; Pineda et al., 1998).

Another explanation behind unique errors is that they reflect delusional thinking in participants in that participants perceive non-existent rules and patterns between the test card and a selected deck. Indeed, a few studies report that patients with schizophrenia commit more unique errors than the general population (Kawasaki et al., 1993; Mattes, Cohen, Berg, Canavan, & Hopmann, 1991; Rossi et al., 2002). One study also found increased unique errors in first- and multiple-episode manic depressive disorder, with many patients in this study being on anti-psychotic medication (Fleck, Shear, Madore, & Strakowski, 2008). SSRIs, which in some cases can cause psychotic symptoms such as hallucinations (Lai, 2012; Schuld, Archelos, Friess, & Bourgeois, 2000), may have propelled schizotypy-like responding on this task in medicated patients. This is, nonetheless, purely speculative as I did not measure any psychosis-related symptoms in this sample to test this theory. Moreover, no patients exhibited any psychotic symptoms when screened prior to study enrolment.

Medicated patients in my study additionally revealed slow response times on the task, which is reminiscent of research identifying slower goal-directed planning in youths with OCD (Huyser et al., 2010; Kim et al., 2018). Computational modelling studies have also highlighted that children with OCD engage in slower and more cautious decision-making compared to healthy children making (Erhan et al., 2017; Hauser et al., 2017), which has been linked to higher levels of subjective uncertainty experienced by patients. This uncertainty drives patients to accumulate more evidence than necessary to reach a decision. Medicated patients in my sample may have felt increased uncertainty surrounding rules present in the WCST, resulting in slower decisions/increased response times. Despite this more careful responding, medicated patients still committed more unique errors, which is consistent with research showing that young patients show comparable or even worse performance on planning tasks compared to healthy children despite slower latencies (Negreiros et al., 2019).

All in all, it is difficult to interpret the results for medicated patients as prior studies administering the WCST to youths with OCD have not analysed unique errors or response times (the latter likely due to the WCST being a self-paced task) (Andrés et al., 2007; Baykal et al., 2014; Beers et al., 1999; Bohon et al., 2020; Geller et al., 2018; Kodaira et al., 2012; Ornstein et al., 2010; Shin et al., 2014; Taner et al., 2011). Hence, I cannot ascertain whether this pattern of results is commonly found in medicated youths with OCD. These measures were included in this current study to discern a more

complete performance profile on the WCST, and they are often included in research studying other populations (e.g. Horowitz-Kraus, 2014; Lie, Specht, Marshall, & Fink, 2006; Somsen, 2007; Somsen, Van Der Molen, Jennings, & Van Beek, 2000). Moreover, majority of research into paediatric OCD reported no medication effects. To my knowledge, only Gruner et al. (2012) has found that medicated children with OCD completed less categories on the WCST compared to unmedicated and control groups. However, a separate study by Andrés et al. (2007), in contrast, found no effect of medication on paediatric OCD WCST performance. Even within the adult literature, OCD patients medicated with SSRIs are reported to display superior performance to unmedicated patients on deterministic reversal learning (Apergis-Schoute et al., in prep), goal-directed planning (Lochner et al., 2020), and during probabilistic reward and punishment learning (Palminteri et al., 2012). Relevant to the current study, adult patients medicated with serotonin reuptake inhibitors (SRIs) show similar performance on the WCST compared to non-medicated patients (Mataix-Cols, Alonso, Pifarré, Menchón, & Vallejo, 2002), suggesting no effect of serotonergic medication on performance. However, this particular study did not include measures of unique errors and response times.

Inversely, there is evidence for acute low dose SSRIs impairing learning and flexibility in healthy participants (Skandali et al., 2018), and for serotonin depletion improving these functions (Scholes et al., 2007). In line with this, and very intriguingly, medication dosage correlated with IQ scores in my study suggesting that receiving a lower dosage of SSRIs impacts performance on intelligence tests. However, SSRI dosage was not correlated with unique errors or response times so it is uncertain whether dosage influenced abnormal performance in medicated adolescent patients.

Ultimately, further research with larger samples of medicated and unmedicated adolescents with OCD investigating unique errors and response times on the WCST is needed to draw any firm conclusions. Larger samples will also enable us to determine whether these specific task deficits are features of ‘pure’ OCD or whether they are only pronounced in the presence of SSRIs.

Further discussion surrounding effects of SSRI medication on cognition are present in Chapters 3,4, and 7 of this thesis.

2.5.3 Computational Modelling

Next, computational modelling analyses implemented here unexpectedly detected no group differences in latent behavioural process on the task. Again, as this is the first study to implement modelling of WCST data in OCD, I am unable to determine whether these results are to be expected. Unlike previous computational modelling research in paediatric OCD, my study found no evidence

of increased exploration [operationalised via the decision-consistency parameter (*d*)] compared to healthy controls. This may be due to the deterministic nature of the task. Most other computational studies modelled tasks with probabilistic pay-offs (Carlisi et al., 2017; Hauser et al., 2017; Kanen et al., 2019; Norman et al., 2018), which incorporate more uncertainty into the tasks' structures. The WCST does not tap into uncertainty in the same way and hence patients do not engage in exploration. There were no differences in model parameter values even when dividing the OCD group by medication status, and despite standard analyses revealing more unique errors in medicated patients. However, this is likely due to unique errors not being captured in the model, as proportion of unique errors did not correlate with any model parameters.

At first obsessive-compulsive severity within the OCD group presented a noteworthy relationship with model parameters; where more severe patients had increased punishment rates and higher decision-consistency. However, when controlling for the effects of age (which correlated highly with task measures and OCI scores) these relationships ceased to be significant.

In contrast, obsessive-compulsive traits in the healthy control group showed more robust relationships with the model parameters, wherein OCI scores (not confounded by age and IQ) predicted lower punishment rates, higher reward rates, and lower decision-consistency. Lower decision consistency in controls with greater obsessive-compulsive traits is consistent with previous research suggesting that OCD is linked to lower perseveration and higher exploration (Fradkin, Ludwig, Eldar, & Huppert, 2020; Hauser et al., 2017; Norman et al., 2018). However, higher reward rates in this sample are unexpected as adult patients with OCD are often found to show reduced activity in brain areas related to reward processing such as the nucleus accumbens and limbic regions (Figee et al., 2011; Wi Hoon Jung et al., 2013). Lower punishment rates are also inconsistent with past studies revealing that adult OCD patients are more punishment sensitive (Endrass et al., 2011; Morein-Zamir et al., 2013; Nielen, Den Boer, & Smid, 2009). Nonetheless, although it appears that controls with obsessive-compulsive traits are updating internal values for each dimension more following rewards compared to punishment, their actions are not consistent with these value changes as demonstrated by their tendency to explore more (lower decision-consistency). This suggests a mismatch between choice value and action in controls with obsessive-compulsive traits.

All things considered, the correlational data are too premature to draw conclusions from as the relationships between obsessive-compulsive traits and parameter values in the control group do not appear in the actual clinical sample, and hence are not generalizable to the general population of youths with OCD. Nevertheless, it is of particular interest to note that this pattern of results (high

reward rate, low punishment rate, and more exploration) mirror the experimental findings in Chapter 6 where I modelled data from a probabilistic reversal learning task obtained from a much larger sample of adolescents with OCD. I discuss these findings in more detail in the discussion section of that chapter.

2.5.4 Limitations and further research

A limitation of this study is that the OCD group's sample size may have been too small to draw solid conclusions, especially when the group is further divided by medication status.

Next, while I used a very well-validated model to decompose behaviour on the WCST, I did not consider other models that may have captured the data better. For instance, I did not fit the trial-by-trial reaction time data to any models. Future research should consider fitting a wider variety of models that may be more informative of behaviour on this task.

Lastly, I did not conduct any neuroimaging of participants due to time constraints within the PhD programme. As mentioned previously, abnormalities may be present in brain activity in young patients but be not pronounced in task behaviour yet. A recent study showed perseverative errors on the WCST in adolescents with OCD, but not in healthy controls, correlated with activity in the frontal lobes, including the right frontal pole and inferior frontal gyrus (Bohon, Weinbach, & Lock, 2020). While fascinating, Bohon et al.'s study employed a relatively small sample of only 11 OCD patients, hence it may be worth revisiting this task as a possible fMRI paradigm administered to a larger sample of patient participants.

2.5.5 Conclusion

Consistent with previous literature, adolescents with OCD do not display a cognitive flexibility deficit on the WCST. Patients medicated with SSRIs showed increased unique errors and slower response times compared to unmedicated patients and controls. It is uncertain whether SSRIs are driving either poorer learning and attention, increased evidence accumulation, or increasing delusional thinking in this sample. While computational modelling revealed no differences in latent task behaviour between groups, obsessive-compulsive severity (measured via the OCI) showed a significant relationship with model parameters within the control group, but interpretation is difficult as these relationships were not present in the OCD group. All in all, findings support generally intact flexibility in adolescents with OCD which is in contrast to most research studying adult patient populations.

Chapter 3: Pavlovian-to-Instrumental Transfer in Adolescents with OCD

3.1 Introduction

Harm avoidance has been proposed to be one of the factors driving compulsive behaviour in OCD (Rasmussen & Eisen, 1990, 1992), wherein compulsions are practiced to prevent incoming danger, harm, and unpleasant thoughts. Indeed, the majority of youths with OCD experience increased harm avoidance as measured via self-report rating questionnaires (Bey et al., 2017; Cervin et al., 2020; Ecker & Gönner, 2008; Ettelt et al., 2008). Moreover, I speculate that threat or harm sensitivity could be linked to adult (see Riesel, 2019 for review) and paediatric (see Marzuki et al., 2020 for review) patients' tendency to display overactive ACC error signals when committing errors on conflict detection paradigms.

Lately, research has shown that a strong propensity for harm avoidance could be linked to disrupted goal-directed behaviour in adults with OCD. Gillan et al. (2014) administered a shock avoidance task where participants were trained to avoid shocks associated with specific computer images by pressing a foot pedal. During devaluation (where the electrodes delivering shocks were disconnected), patients with OCD still made more foot pedal responses than control participants to the images previously associated with a shock. It was inferred that patients with OCD formed a strong habitual avoidance response and failed to adjust their behaviour in a goal-directed manner. This particular study found results pertaining to instrumental learning (stimulus – outcome – response association), but a later study by Apergis-Schoute and colleagues (2017) found that Pavlovian learning (stimulus – outcome association) is also abnormal in adults with OCD. Experimenters trained adults with OCD and healthy adults on a shock avoidance task while collecting participants' skin conductance response (SCR) data. SCR or sweat levels represent arousal and are widely used as a measure of aversive Pavlovian learning (Esteves, Parra, Dimberg, & Ohman, 1994). All participants differentiated between stimuli that predicted shock and neutral stimuli, however following reversal of threat contingencies, patients did not update their SCR to differentiate between the newly safe and unsafe stimuli. Both studies suggest that adults with OCD have difficulty inhibiting threat responses possibly due to an amalgamation of enhanced harm avoidance and a bias towards habitual responding.

Similarly, paediatric OCD patients are thought to be impaired in inhibiting Pavlovian fear responses as young patients have been found to display persistently large SCRs to stimuli that were previously associated with threat (loud noises) despite them now being safe (Geller et al., 2017). Moreover,

young patients have also been reported to display abnormal SCR differentiation in general: McGuire et al. (2016) found that patients' initially demonstrated the expected high and low SCRs towards a threatening conditioned stimulus (CS+) and a safe conditioned stimulus (CS-) respectively. But after extinction, their SCRs paradoxically decreased towards CS+ and increased in response to CS-. This aberrant differentiation in SCRs suggests that children with OCD display impaired adaptation towards Pavlovian conditioned cues. Additionally, poor SCR differentiation predicted worse cognitive behavioural therapy outcomes for children with OCD (Geller et al., 2019). This indicates that a proportion of children with OCD are unable to retain implicit contingency learning under extinction. An alternative explanation related to harm avoidance is that children with OCD 'reset' their learning in ambiguous contexts (in this case under extinction) as it is unclear to them which CS would be associated with the threatening unconditioned stimulus (US). Heightened anxiety may be driving these responses in children with OCD, as patients with anxiety disorders also show abnormal differentiation between CS+ and CS- on fear conditioning paradigms (Duits et al., 2015). All in all, adult OCD appears to be distinctly associated with maladaptive habitual avoidance responding while evidence thus far suggests abnormal fear learning in children with OCD.

Recently, Pavlovian-to-Instrumental Transfer (PIT) paradigms have been employed to understand how Pavlovian cues influence learnt instrumental actions to seek rewards or avoid punishment (Cartoni, Balleine, & Baldassarre, 2016). Typically, the PIT task involves 3 key stages: the instrumental phase, Pavlovian phase, and Pavlovian-to-instrumental transfer (PIT) phases. In animal PIT studies (as described in detail by Cartoni et al. (2016)), the instrumental phase involves establishing a relationship between distinct actions and outcomes, such as pressing lever A for sucrose, and lever B for a food pellet. This phase is then followed by the Pavlovian phase which requires subjects to implicitly learn stimulus-outcome associations, for example learning that unique auditory tones (conditioned stimuli, CS) predict the delivery of different food outcomes (unconditioned stimuli, US). The outcomes used in the instrumental phase are re-used in this phase alongside a brand new reward (e.g banana slices). Hence 3 different CSs would uniquely predict the delivery of the three separate outcomes. Lastly, the PIT phase would be conducted to probe the motivational influences of CS over the learned responses from the instrumental phase. This phase would be performed under extinction, meaning the CS no longer predicted learnt outcomes. Behaviour from this last phase can model two PIT processes – specific and general transfer. Specific transfer refers to the selective effect of CS on responses related to the same outcome. Using the above example, animals are thought to demonstrate a specific transfer when the tone predicting sucrose enhances their responses for the sucrose-producing lever only. By contrast, a general transfer

involves an overall motivational influence of the CS on instrumental responding. Again using this example, a general transfer is said to occur when the tone predicting the delivery of a banana slice (which is not involved in initial training) enhances responding for both sucrose and food pellet levers.

It is thought that specific transfer reflects previous action-outcome learning while general transfer depends solely on the valence of the Pavlovian (CS) cue. We can observe examples of specific and general transfer in daily human life; seeing an advertisement for a particular clothing brand may elicit the desire to purchase an item belonging to the brand in question (specific transfer) as well as increase motivation to shop for other goods or from other stores (general transfer). In terms of studying psychopathology, the PIT paradigm is often utilised in addiction research to understand how Pavlovian cues (such as sounds coming from a pub) enhance desire for the consumption of drugs and alcohol (Garbusow et al., 2019; Hogarth et al., 2019; van Timmeren et al., 2020). There has been less consideration for how PIT effects are associated with the maintenance of obsessive-compulsive symptoms. Contrasting with an appetitive PIT, which enhances desirable or motivational aspects, Pavlovian cues might modulate aversive aspects of a stimulus, thereby heightening patients' desire to seek safety or avoid harm. This is in line with the aforementioned harm avoidance model of OCD. For instance, a person with OCD whose worries and urges revolve around disease and injury may be triggered to seek reassurance or wash themselves compulsively when close to potentially contaminated areas or when watching news reports of disease outbreak on television.

Relevant to the previous discussion of goal-directed and habitual behaviour, PIT tasks can probe how goal-directed outcome-response associations established in the instrumental phase transform to become habitual stimulus-response associations in the PIT phase (Garofalo & Robbins, 2017), as responses here are conducted under extinction. Additionally, it is reported that separate learning mechanisms underlie the types of transfer in the task, whereby specific PIT reflects more model-based behaviour as it involves the matching of the correct instrumental response to a conditioned stimulus in order to achieve a desired outcome, while general transfer is elicited from the implicit motivational properties of the Pavlovian cue, and is hence more reflective of model-free behaviour (Dolan & Dayan, 2013). Concretely, specific transfer has been discovered to be associated with higher order cognitive skills but not general transfer (Garofalo, Battaglia, & di Pellegrino, 2019).

Some authors propose that the lateral OFC and its projections into striatum underlie the ability to successfully use Pavlovian cues to guide specific instrumental actions (Balleine & O'Doherty, 2010; Ostlund & Balleine, 2007). Hence, it may be that adults and children with OCD, who generally show reduced or disrupted lateral OFC functioning (Chamberlain et al., 2008; Remijnse et al., 2006; Rotge

et al., 2008; Woolley et al., 2008), would be less accurate at integrating the instrumental and Pavlovian influences necessary to conduct specific transfer on PIT paradigms. Moreover, as described in other sections of this thesis, children and adolescents with OCD are reported to be impaired in both instrumental and explicit learning (Gottwald et al., 2018; Vloet et al., 2010), suggesting that young patients may be unable to adequately learn the fundamental instrumental and Pavlovian contingencies needed for specific transfer. Hence, they may only be able to show general transfer, which is a cognitively simpler action supposedly tapping into model-free processes.

Only one published study hitherto has explored PIT in relation to OCD. Using an aversive PIT task, Krypotos and Engelhard (2020) found that healthy adults with high obsessive-compulsive traits displayed less specific transfer responses compared to adults with lower traits indicating that the high trait group were worse at generalising learnt associations during the PIT phase. It can be inferred that this deficit is associated with decreased model-based behaviour as well as reduced lateral OFC functioning in populations with OCD (Voon, Baek, et al., 2015; Voon, Derbyshire, et al., 2015; Wheaton et al., 2019). No differences in general transfer were seen between high trait and low trait adults in Krypotos and Engelhard's study, further demonstrating greater model-free reliance in this population.

In this current study, a PIT task previously employed by Garofalo and Robbins (2017) was administered to adolescents with OCD and healthy matched controls. The PIT task used was aversive in nature to probe instrumental and Pavlovian processing, as well as specific and general transfer under fearful contexts in the adolescents with OCD. Loud aversive sounds were used as the USs as this type of stimuli has been successfully used in prior fear conditioning experiments involving children with OCD (Geller et al., 2017; McGuire et al., 2016). Participants were instructed to learn to avoid the noises by moving a joystick in the correct direction. It was hypothesised that adolescents with OCD would show weaker specific transfer reflecting reduced model-based control and lateral OFC dysfunction in this population, but intact general transfer, similar to Krypotos & Engelhard's (2020) findings. Furthermore, as harm avoidance is prevalent in those with OCD, I hypothesised that adolescent patients would display increased responses overall during the Instrumental and PIT phases compared to healthy adolescents as patients may be more motivated to avoid the aversive stimuli.

3.2 Methods

3.2.1 Sample

Originally, 41 participants (21 CTl, 20 OCD) were projected to complete this task, however 1 participant with OCD was tested outside of Cambridge and was not able to come to the laboratory to be administered the PIT task. Another control participant was not able to complete the task due to equipment failure. Hence, thirty-nine participants completed the PIT task, with 19 adolescents diagnosed with OCD forming the OCD group and 20 healthy adolescents forming the CTL group. Eleven adolescents with OCD were receiving SSRI treatment when they completed the task while 8 were medication-naïve. Out of the 11 medicated patients, 8 were receiving sertraline while 3 were receiving fluoxetine. Mean SSRI dosage was 97.27 mg (s.d. 58.33) and the dose ranged from 20 mg to 200 mg. IQ and digit span data was missing from one OCD participant. Further demographic details are outlined in the Results section of this chapter.

3.2.2 Equipment

To collect skin conductance responses (SCR) during the PIT task (see Procedure below), I attached Vermed disposable Galvanic Skin Response snap electrodes to each participants' fingertips (middle and index fingers) on their non-dominant hands. These electrodes were connected to a DC amplifier (Biopac Systems –MP150 – GSR100). A gain factor of 5 µS/V and low-pass filter set at 0.05 Hz were used for recording the analogue signal, which was then passed through the digital converter at a 200 Hz rate. The signal was fed into AcqKnowledge 3.9 (Biopac Systems). During certain phases of the task, participants were instructed to respond to stimuli by moving a joystick left or right. An isometric hand dynamometer (Biopac Systems—MP150—TSD121C—DA100C) attached to the base of the joystick was used to record hand grip compression (vigour) responses from participants. A transducer inserted inside the joystick converted grip pressure into signals fed into AcqKnowledge 3.9. Participants were told to squeeze the joystick, where the transducer was located, every time they moved the joystick left or right.

3.2.3 Procedure

Participants were seated in front of a desktop screen with a joystick located on the table in front of them. They were required to wear headphones throughout the task, as well as electrodes on their middle and index fingertips to record their SCRs (see Figure 3.1). Before beginning the task, the volume of the unpleasant noises was calibrated according to individual tolerance levels. We advised each participant that the noises would be irritating without being at all painful. Participants completed the task in a silent room with no distractions.

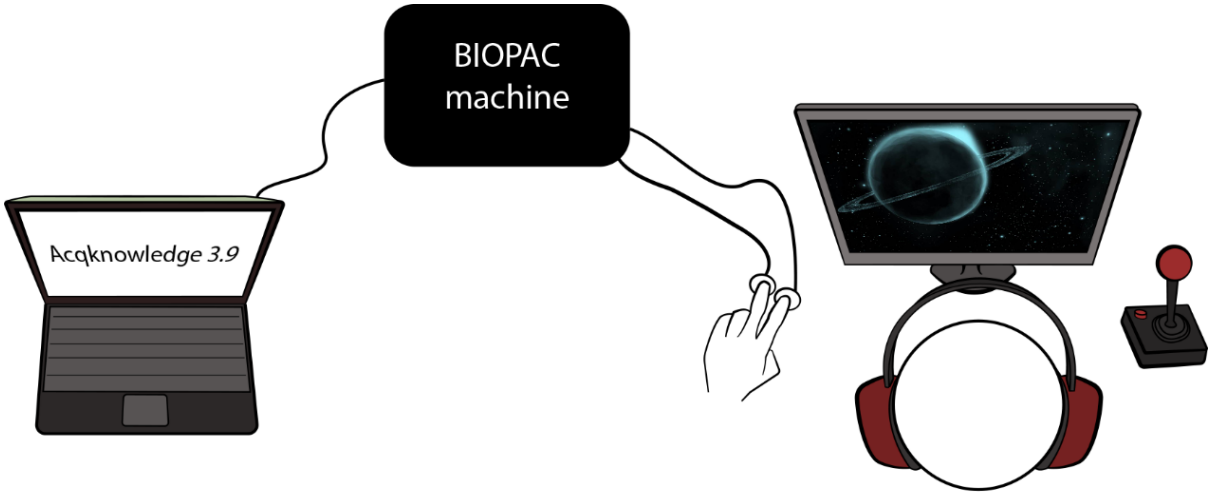

FIGURE 3.1: SET-UP OF EQUIPMENT FOR PAVLOVIAN-TO-INSTRUMENTAL TRANSFER STUDY. PARTICIPANTS WERE SEATED IN FRONT OF A DESKTOP COMPUTER WEARING HEADPHONES. THEY USED A JOYSTICK (CONNECTED TO A HAND DYNAMOMETER TO MEASURE GRIPPING FORCE) TO INTERACT WITH THE TASK. ELECTRODES WERE ATTACHED TO THE PARTICIPANTS' INDEX AND MIDDLE FINGERTIPS TO MEASURE SCRS. SCR SIGNALS WERE FED THROUGH A BIOPAC DC AMPLIFIER AND DATA WAS COLLECTED ON A SEPARATE LAPTOP RUNNING ACQKNOWLEDGE 3.9 SOFTWARE.

3.2.4 Pavlovian-to-Instrumental Transfer Task

The task consisted of 3 experimental phases, namely Instrumental Conditioning, Pavlovian Conditioning, and the PIT phases, which are described in detail below. The entire task was presented using the software Presentation (Neurobehavioral Systems, Albany, CA, USA).

Phase1: Instrumental Conditioning

The aim of this phase was to train participants to create an instrumental association between goal-directed responses (moving the joystick left or right) and unconditioned stimuli (two aversive noises labelled US1 and US2). We used a 'Space Mission' narrative to keep participants engaged throughout the task. They were told that they were currently under attack on their mission, and their goal was to avoid being hit by two possible attacks, namely 'bombs' and 'missiles' presented as cartoon images on screen. Each attack was associated with 1 of 2 aversive noises (either US1 or US2) played at the same time as the image. Participants were told they could avoid hearing the noises if they moved the joystick in time either to the left or right. They were also told that there was a preferred direction that could stop each attack.

During the game (see Figure 3.2), each trial began with a visual message displaying "defend yourself" for 2s alongside an image of the US (bomb or missile) that was about to come. For the following 30s in the trial, only one of the possible USs would be displayed following a random time schedule (every

1.5s – 3s). If participants successfully moved the joystick in the correct direction, they would be shown an image displaying 'Avoided' for 1s and no noise would be delivered. USs were able to be avoided by moving the joystick the correct way only 80% of the time, but participants were not told of this. Instead, they were advised that if an attack still occurred despite moving in the correct direction, it was due to them not squeezing the joystick with enough strength.

Before beginning the instrumental conditioning phase, participants first completed a training session with 4 trials that was identical to the actual phase except without any noises delivered whenever they were 'hit'. During the real phase, participants underwent 8 trials in total (4 trials featuring US1 and 4 trials featuring US2). The duration of the phase was approximately 8 minutes. The association between instrumental response (left/right) and type of attack (US1/US2) was counterbalanced across participants. At the end of this phase, I assessed explicit learning by asking participants to pair each US with its corresponding avoidance responses. Participants also rated how confident they were in their pairings on a scale from 1-9. Lastly, they were instructed to rate how much they wanted to avoid the attacks on a scale from 1-9 (as a measure of level of aversion).

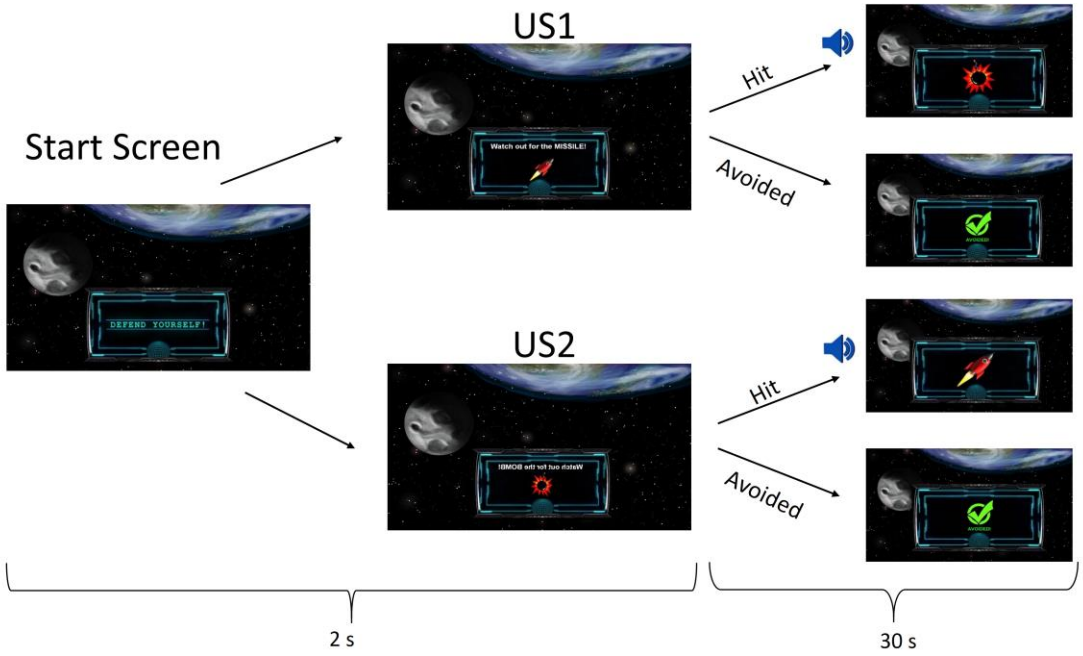

FIGURE 3.2: PRESENTATION OF 1 TRIAL DURING THE INSTRUMENTAL PHASE. PARTICIPANTS WERE ABLE TO RESPOND AS MUCH AS THEY WANTED WITHIN A 30 SECOND WINDOW. THEIR GOAL WAS TO LEARN TO MOVE THEIR JOYSTICK IN THE CORRECT DIRECTION TO AVOID BEING 'HIT'.

Phase 2: Pavlovian Conditioning

In this phase, I aimed for participants to passively learn the associations between different images and USs. Before beginning this phase, participants rated on a scale from 1-9 how much 4 different images of outer space appealed to them. These 4 images were later used as conditioned stimuli (CS). Participants were presented with new instructions informing them that they would 'travel across different galaxies' while still experiencing attacks. The two USs from the Instrumental phase were re-used here, alongside one new US featuring an image of dynamite and a different aversive noise (US3). Moreover, participants were told that due to malfunction, they would no longer be able to use the joystick to defend themselves against the attacks. Their goal now was to gather information to further their mission, namely by learning which US was presented most frequently alongside each CS (see Figure 3.3).

There were 68 trials in total (17 trials for each of the 4 CS/images), and the phase lasted 15 minutes in total. In each trial, one of the 4 CS were presented to participants followed by either the US (aversive noise + image of attack, either bomb, rocket or dynamite) or a message saying 'Avoided'. These outcomes lasted 1s and were presented 4.5s after CS onset. In between trials, there was a variable interval ranging from 7s-9s. Two of the scenes (CS1 and CS2) were paired with US1 and US2 from the Instrumental phase, while CS3 was paired with the new US3. The fourth scene (CSm) was not associated with any noise, and always displayed 'Avoided' when presented on screen. The pairings of different USs with CSs was counterbalanced across participants.

After the phase concluded, participants were asked to explicitly tell the experimenter which CS was paired with each US. Participants also rated how confident they were in their pairings on a scale from 1-9. In addition, participants rated once more on a scale from 1-9 how much the space scenes appealed to them.

FIGURE 3.3: IMAGES OF SPACE WERE USED AS THE CS IN THE PAVLOVIAN PHASE. DIFFERENT UNPLEASANT SOUNDS (US) WERE DELIVERED DEPENDING ON THE CS BEING PRESENTED. THE NEUTRAL CS (CSM) HAD NO NOISE PRESENTED ALONGSIDE IT.

Phase 3: Pavlovian-to-Instrumental Transfer

Here, we aimed to test the ability of Pavlovian cues (CSs) to trigger instrumental avoidance responses even when they were no longer associated with any aversive US (under extinction). This phase was identical to the Instrumental Conditioning phase except the aversive noises were no longer delivered and images of the attacks (bomb, missile, dynamite) were no longer presented. Images of outer space that previously served as different CSs were presented in the background of each trial (see Figure 3.4).

At the beginning of this phase, participants were told that their joystick had resumed working, and that they could use it to defend themselves again. However, they would no longer be told at the start of each trial what attack was about to come. They were told that they should still respond with the joystick to avoid any possible attacks. In reality, no noises were delivered throughout the entire phase. Participants underwent 6 trials for each CS condition (a total of 24 trials) and for a duration of approximately 10 minutes.

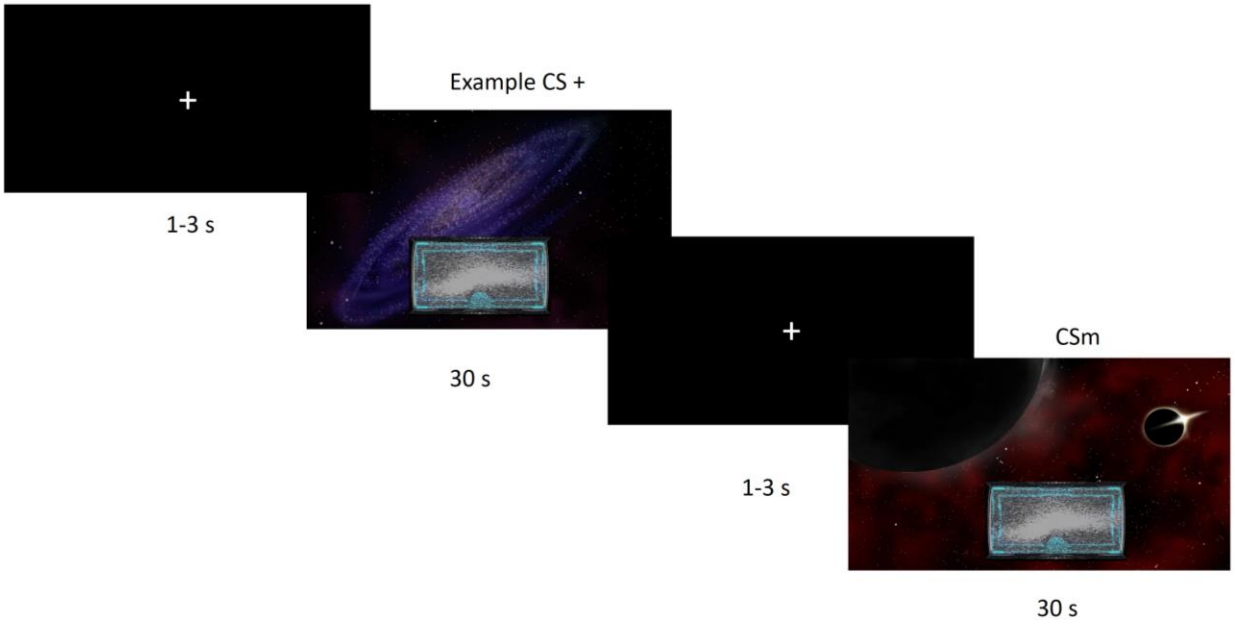

FIGURE 3.4: STIMULUS PRESENTATION DURING THE PIT PHASE. PARTICIPANTS WERE TOLD TO RESUME RESPONDING USING THE JOYSTICK WHEN PRESENTED WITH DIFFERENT CS, BUT THEY WERE NOT TOLD THAT NO NOISES WOULD BE DELIVERED IN THIS PHASE.

3.3 Statistical Analyses

Analyses and data cleaning were conducted using AcqKnowledge 5.0, Matlab R2017b, and RStudio 3.5.

Prior to all analyses, the Levene's test was used to assess homogeneity of variance while the Shapiro-Wilke's test was used to assess normality.

3.3.1 Instrumental Conditioning Phase

Learning was assessed in this phase by examining the effects of US (US1 & US2) and Group (CTL & OCD) on percentage of correct responses (whenever a participant moved the joystick in the reinforced direction for each US) made. Due to violation of the normality assumption, a non-parametric version of a mixed-Analysis of Variance (ANOVA) that uses approximate degrees of freedom called the mixed Welch-James from the 'welchADF' package in RStudio (Villacorta, 2017) was used to assess this and other measures reported below. The main test statistic is the T_{WJ} similar in interpretation to the F statistic that is output from conducting standard ANOVAs. Generalised eta-squared (η2G) values were calculated and reported as measures of effect size, with 0.02, 0.13, and 0.26 being cut-off values for small, medium, and large effect sizes respectively.

To measure any distinctions in urges to avoid the USs between groups, a further Welch-James test was conducted with mean number of responses as the dependent variable and with Group and US as independent variables. If one group had more of an urge to avoid the US, the mean responses made by that group would be higher. Likewise, if one US was considered more aversive than the other, it would elicit an increased number of responses.

I investigated how accurate groups were in explicitly reporting which US was paired with which response using a Fisher's exact test for count data. Participants' confidence ratings for this explicit association test were analysed using a Welch-James test with Group and US as independent variables.

Explicit ratings of urge to avoid USs were analysed using a rank-sum Wilcoxon test. Confidence and urge ratings were converted to proportions by dividing each raw score by 9 (which is maximum rating on the scales).

3.3.2 Pavlovian Conditioning Phase

The only behavioural data collected in this phase were liking ratings of CSs before and after Pavlovian trainings, an explicit CS-US associations test, and confidence ratings of explicit CS-US associations. Group differences in CS-US explicit associations per CS-type were analysed using Fisher's exact test. Confidence and liking ratings were converted to proportions by dividing each raw score by 9 (maximum rating on the scales). Confidence ratings were analysed using a mixed Welch-James test with Group and US as independent variables. Liking ratings were also analysed using a mixed Welch-James test with Group as the between-subjects' variable, and CS (CS1, CS2, CS3, CSm) and time (before and after Pavlovian training) as the within-subject variables. Post-hoc Wilcoxon tests with Bonferroni correction were used for post-hoc comparisons of liking ratings between the different CSs.

3.3.3 SCR Analysis

SCR analyses were only conducted in the Pavlovian phase to determine whether subjects had learnt to implicitly distinguish between the aversive CSs and CSm. SCRs were not analysed in the Instrumental and PIT phases as the movement of the joystick during data acquisition resulted in artefacts in the SCR data.

Following data collection, peak-to-peak amplitude of event-related SCR signals were extracted using Autonomate version 2.8 (Green, Kragel, Fecteau, & LaBar, 2014) which was run as a toolbox in Matlab R2017b. Autonomate was used as it is a straightforward method of analysing SCR amplitude enabling automatic data pre-processing (using down sampling, which reduces the sampling rate in order to decrease the effect of high frequency noise on subsequent analysis), SCR identification,

isolation of overlapping responses, and amplitude output. The time window for the peak-to-peak amplitude of the largest signal deflection was set at 0.5s - 4.5s after the onset of each stimulus. The detection slope (minimum slope amplitude required to be coded as a SCR) was set at 0.02 μS/s. Default values provided by Autonomate were used for all other parameters: the detection length (minimum length of the rising period for a potential response to be considered valid) was 0.7s, the down sampling factor (by which the input data are down sampled prior to analysis) was 25, the buffer length (the size of the search window applied to the beginning and end of valid response periods of the down sampled data when looking for the response trough and peak in the non-down sampled data) was 0.125, maximum responses (maximum number of responses that can be detected in a time window before the data are considered too noisy for analysis) was set at 8, and the sampling rate was set at 200Hz.

After processing using Autonomate, individual SCRs were z-transformed using the average and standard deviation of each subject's SCR amplitudes over the entire Pavlovian phase (as was previously done by Gillan et al., 2014) For each participant, the first 9 trials were collapsed and designated 'Block 1' while the last 8 trials were collapsed and designated 'Block 2'. To investigate learning over time using SCRs, a mixed-ANOVA was used to assess mean z-scored SCR amplitudes with Group as a between-subjects' variable, and Block (1 and 2) and CS (CS1, CS2, CS3, CSm) as within-subject variables. If participants implicitly learnt the associations between CSs and USs, I expected to observe increased SCR over time for CSs 1,2, and 3, and decreased SCR over time for CSm.

3.3.4 PIT Phase

Specific PIT was investigated by exploring only the effects of CS1 and CS2 (collapsed) on mean number of responses and force. Responses were classified as congruent (going in the same direction that was reinforced in the Instrumental phase towards the corresponding CS) or incongruent (going in the opposite direction to the one that was reinforced). A mixed Welch-James test was conducted with mean number of responses as the dependent variable, Congruence (Congruent vs Incongruent) as the within-subjects' variable, and group as the between-subjects' variable.

General PIT was investigated by only considering the effects of CS3 and CSm on mean number of responses and force. A mixed Welch-James test was conducted with mean number of responses as a dependent variable, CS (CS3 & CSm) as a within-subjects' variable and Group as a between-subjects' variable.

3.3.5 Grip Analysis

Force measures obtained via grip strength over the hand dynamometer were recorded in kilograms (Kg) and extracted from the continuous signal by calculating the mean maximum amplitude per event per trial. These measures were used as a further measure of general PIT. The data were extracted per subject using AcqKnowledge 5.0. A mixed Welch-James test was conducted on mean force amplitudes with Group as the between-subjects' variable and CS (CS3 & CSm) as the within-subjects' variable. Participants who did not make any responses to either CS3 or CSm, or both were excluded from this analysis.

All analyses were then repeated with OCD split into MED- and MED+ to explore the effects of medication on PIT performance.

3.4 Results

3.4.1 CTL vs OCD

Thirty-nine participants (20 CTL and 19 OCD) completed the Pavlovian-to-Instrumental task. Demographic, clinical, and intelligence scores are summarised in Table 3.1. OCD and CTL were matched for age, gender, and IQ. OCD displayed significantly increased depression, anxiety, and obsessive-compulsive scores compared to CTL.

Table 3.1: Demographic, intelligence, and clinical scores and comparisons

	CTL (n = 20)	OCD (n = 19)	STATISTIC
GENDER (F:M)	13:7	12:7	$\chi 2(1) = 0.014$; $p = .90$
AGE	15.95 ± 2.05	16.29 ± 1.74	t(37) =-0.56; $p = .58$
WASI-II (IQ)[a]	111.75 ± 10.29	107.63 ± 13.96	t(37) =1.05; $p = .30$
Digit Span[a] (Forwards)	11.05 ± 2.63	11.21 ± 2.19	Z = -0.043 ; $p = .97$
Digit Span[a] (Backwards)	8.40 ± 2.44	8.05 ± 1.87	Z = 0.93; $p = .35$
BDI**	45.2 ± 6.89	59.05 ± 9.55	Z = -4.00; $p =$ 6.902e-05
BAI**	47.85 ± 9.55	67.52 ± 10.10	t(26.89) = -7.56; $p =$ 4.00e-08
OCI**	8.85 ± 7.13	30.47 ± 15.31	t(37) = -5.70; $p =$ 1.592e-06
Y-BOCS	N/A	23.32 ± 5.22	N/A

Key: CTL: Control Group; OCD: Obsessive-Compulsive Disorder group; WASI-II: Wecshler's Abbreviated Scale of Intelligence – II; IQ: Intelligence Quotient; BDI: Beck's Depression Inventory (t-scored); BAI: Beck's Anxiety Inventory (t-scored); OCI: Obsessive-Compulsive Inventory; CY-BOCS: Child Yale-Brown Obsessive-Compulsive Scale. *p<.05; **p<.01; [a] missing data from one OCD participant.

Instrumental Conditioning Phase

When assessing learning of the instrumental condition, it was found that CTL (US1: 88.89 ± 15.35; US2: 87.86 ± 16.86) and OCD (US1:89.70 ± 10.97; US2: 88.17 ± 14.79) both showed satisfactory performance (see Figure 3.5). There were no differences in learning between groups (p = 0.90). Additionally, there was no effect of US-type on learning (p = .50). Moreover, most participants responded correctly when asked to explicitly indicate the correct avoidance response for US1 (Participants who responded correctly, CTL: 18/20; OCD:16/19) and US2 (Participants who responded correctly, CTL: 19/20; OCD:16/19). Fisher's tests showed no group differences in explicit rating accuracy for US1 (p = 1.00) and US2 (p = 0.60). There was no difference in confidence ratings between CTL and OCD (p = .84), as well as between confidence ratings for US1 and US2 (p = .33).

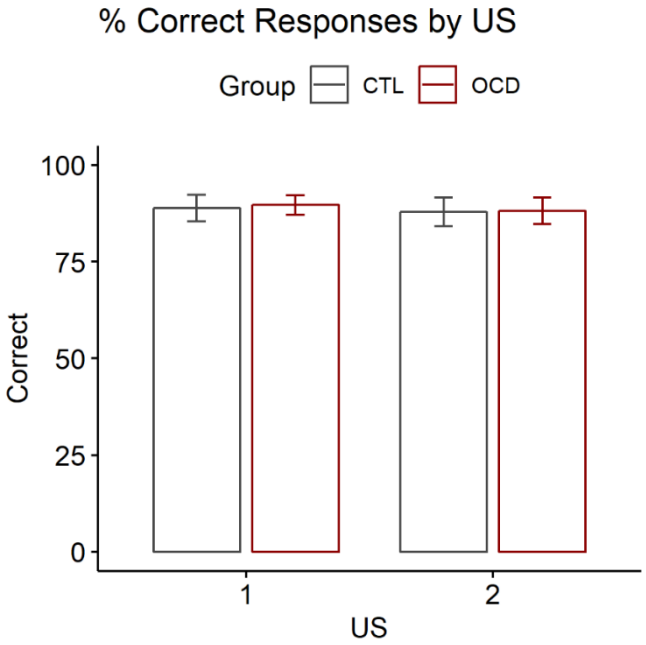

FIGURE 3.5: BOTH CTL AND OCD RESPONDED MOSTLY CORRECTLY TO US1 AND US2 IN THE INSTRUMENTAL PHASE.

Next, there were no differences in number of responses (see Figure 3.6) made towards US1 and US2 (p = .18) or between CTL and OCD (p = 0.66). CTL and OCD were also comparable in their explicit ratings of how much they wanted to avoid the USs (p = .35).

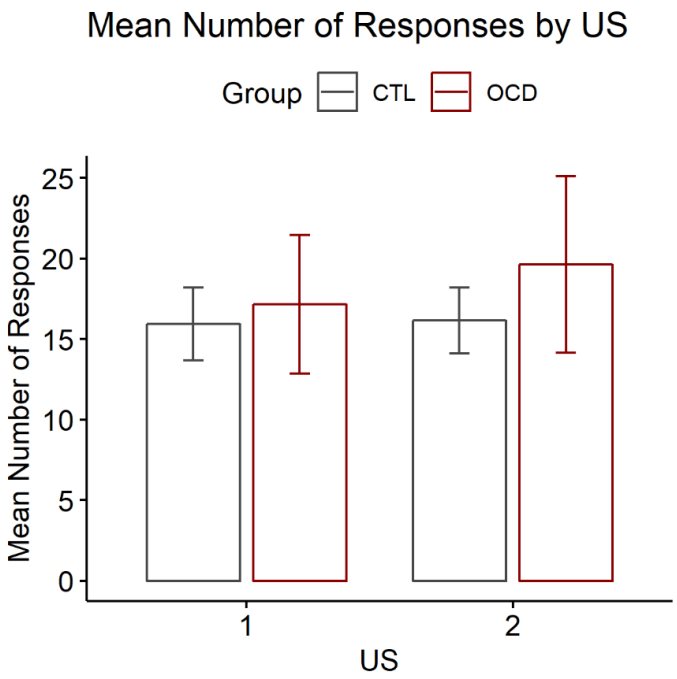

FIGURE 3.6: NO SIGNIFICANT DIFFERENCES BETWEEN GROUPS IN MEAN NUMBER OF AVOIDANCE RESPONSES MADE TO EACH US.

Pavlovian Conditioning Phase

Two CTL participants did not show any SCRs and were hence excluded from this analysis. When considering the mean SCR amplitudes per group and per CS in this phase (see Figure 3.7), the mixed-ANOVA showed a main effect of CS, F (3,102) = 2.95; p = .036; η2G = 0.036. Post-hoc t-tests with Bonferroni correction revealed that overall CS3 elicited greater SCR amplitudes compared to CS2 (t(71) =3.17; p = .014). There were no significant differences in SCRs elicited by CSm compared to any of the CS+s, which made it difficult to ascertain whether participants were implicitly able to discriminate between the neutral and aversive CSs. There was also no main effect of Group (p = .51) or Block (p = .71) on SCRs.

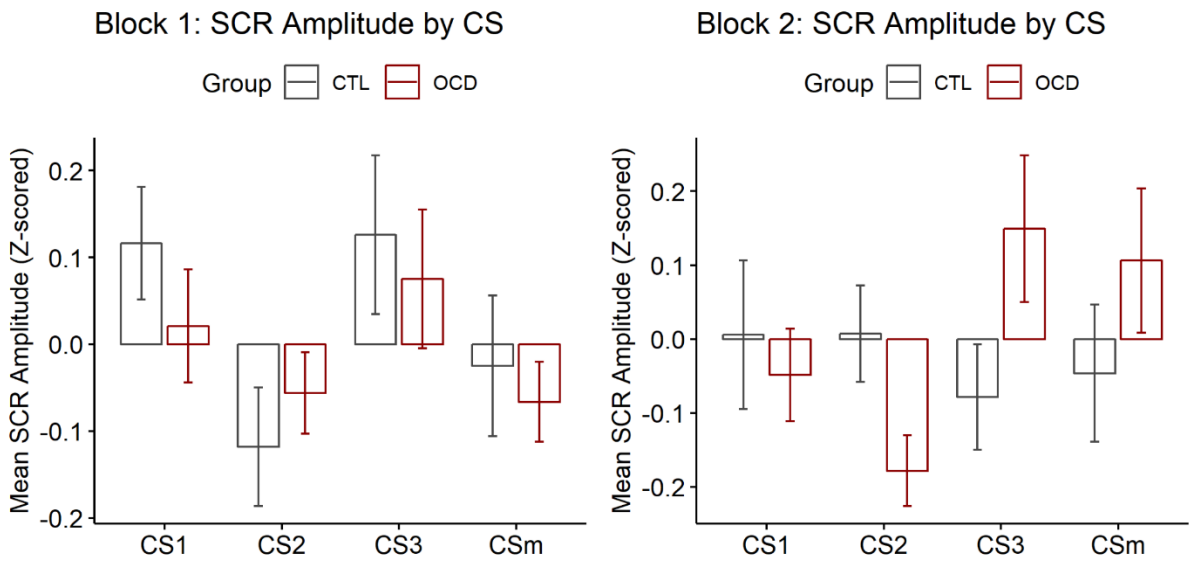

FIGURE 8.7: MEAN Z-SCORED SCR AMPLITUDE FOR THE FIRST HALF OF THE PAVLOVIAN PHASE (BLOCK1) AND THE SECOND HALF (BLOCK 2). OVERALL, THERE WAS A MAIN EFFECT OF CS, WHEREIN POST-HOC TESTS REVEALED CS3 ELICITED SIGNIFICANTLY HIGHER SCRS COMPARED TO CS2. NO OTHER DIFFERENCES WERE FOUND.

Next, I considered participants' explicit responses. One CTL's responses were missing due to software failure. It was found that CTL were able to explicitly associate the US with the CS in this phase (Answered correctly - CS1: 19/19, CS2: 18/19, CS3: 19/19). Most OCD also responded correctly (Answered correctly - CS1: 16/19, CS2: 16/19, CS3: 17/19). Fisher's tests revealed no significant differences in accuracies for each of the CS (CS1: p = .23; CS2: p = .60; CS3: p = .49).

When investigating confidence ratings for this phase, I found a significant main effect of Group ($T_{WJ}(1,22.21) = 9.64$, p = .0051; $\eta 2G = 0.15$), where OCD (0.84±0.20) made lower confidence ratings than CTL (0.96±0.067) – see Figure 3.8. There was also a significant main effect of CS-type ($T_{WJ}(2,19.63) = 3.63$, p = .046; $\eta 2G = 0.038$). Post-hoc paired Wilcoxon tests revealed CS1 elicited lower ratings than CS3 (CS1: 0.87±0.18; CS3: 0.94±0.12; Z = -2.18, p = .029). There were no differences in ratings elicited between CS1 and CS2 (CS2: 0.91±0.17; p = .16) and between CS2 and CS3 (p = .91).

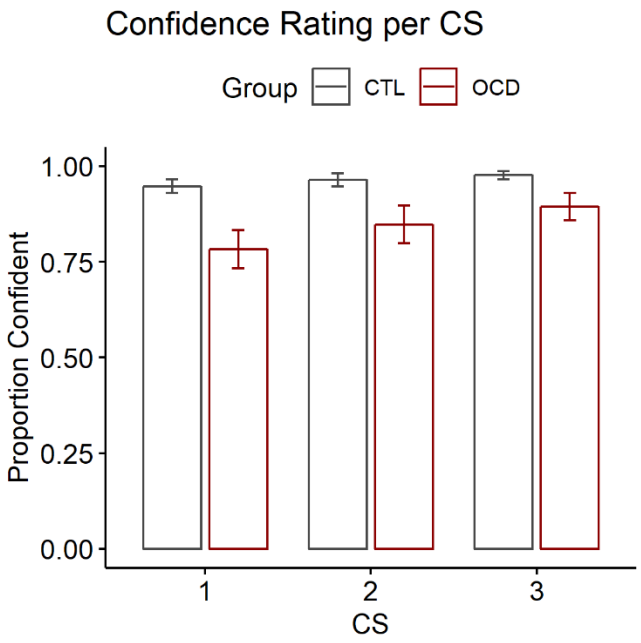

FIGURE 3.8: CONFIDENCE RATINGS DURING PAVLOVIAN PHASE PLOTTED BY CS-TYPE AND GROUP. OCD DISPLAYED LOWER CONFIDENCE RATINGS REGARDLESS OF CS-TYPE. ADDITIONALLY, OVERALL CS1 ELICITED LOWER CONFIDENCE RATINGS COMPARED TO CS3.

Following this, the Welch-James test investigating liking ratings of the CSs revealed a significant effect of time ($T_{WJ}(1,36.99) = 7.26$, $p = .011$; $\eta 2G = 0.007$) and a time by CS interaction ($T_{WJ}(3,28.93) = 6.60$, $p = .0016$; $\eta 2G = 0.014$). The significant effect of time indicated that liking ratings across the CS decreased from pre-conditioning to post-conditioning. Furthermore, post-hoc rank-sum Wilcoxon tests revealed that CS1 ($Z = 1.30$, $p = .097$), 2 ($Z = 2.53$, $p = .0056$), and 3 ($Z = 2.73$, $p = .0031$), decreased in their ratings from pre- to post- conditioning, but CS- significantly increased in liking ratings ($Z = -2.13$, $p = .017$).

Although results from the SCR analysis were unclear, the explicit associations and liking ratings indicated that participants were, on average, able to learn the CS-US associations.

Pavlovian-to-Instrumental Phase

First specific PIT was assessed (see Figure 3.9). A significant effect of Congruence was found over the mean number responses, wherein more congruent responses were made compared to incongruent responses ($T_{WJ}(1,35.28) = 5.34$, $p = .027$; $\eta 2G = 0.059$). There was no effect of Group ($p = .78$) indicating that both groups showed similar levels of specific PIT transfer.

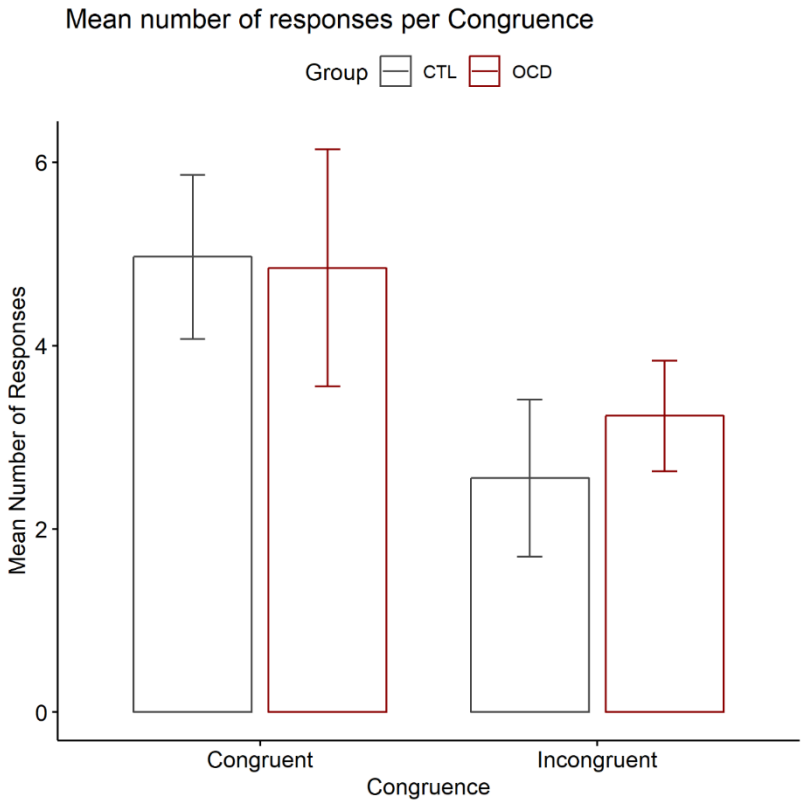

FIGURE 3.9: THE MEAN NUMBER OF CONGRUENT AND INCONGRUENT RESPONSES WERE ASSESSED AS A MEASURE OF SPECIFIC PIT (COLLAPSING ACROSS CS1 AND CS2). PARTICIPANTS MADE MORE CONGRUENT RESPONSES COMPARED TO INCONGRUENT, INDICATING SUCCESSFUL SPECIFIC TRANSFER. THERE WERE NO DIFFERENCES BETWEEN GROUPS.

Next, general PIT was assessed first by measuring the mean number of responses made towards CS3 and CSm (see Figure 3.10). There was a significant effect of CS ($T_{WJ}(1,21.75) = 4.40$, $p = .048$; $\eta 2G = 0.041$) wherein more responses were made in response to CS3 compared to CSm. Next, I considered participants' force data and also found a trend for more force applied to CS3 compared to CSm ($T_{WJ}(1, 27.80) = 4.18$, $p = .051$; $\eta 2G = 0.029$) – see Figure 3.11. Three CTL and 2 OCD were excluded from the force analysis as they did not make any responses to CSm. In both general PIT analyses, there was no effect of Group (number of responses: $p = .56$; force: $p = .56$), indicating that CTL and OCD displayed general transfer to a similar extent.

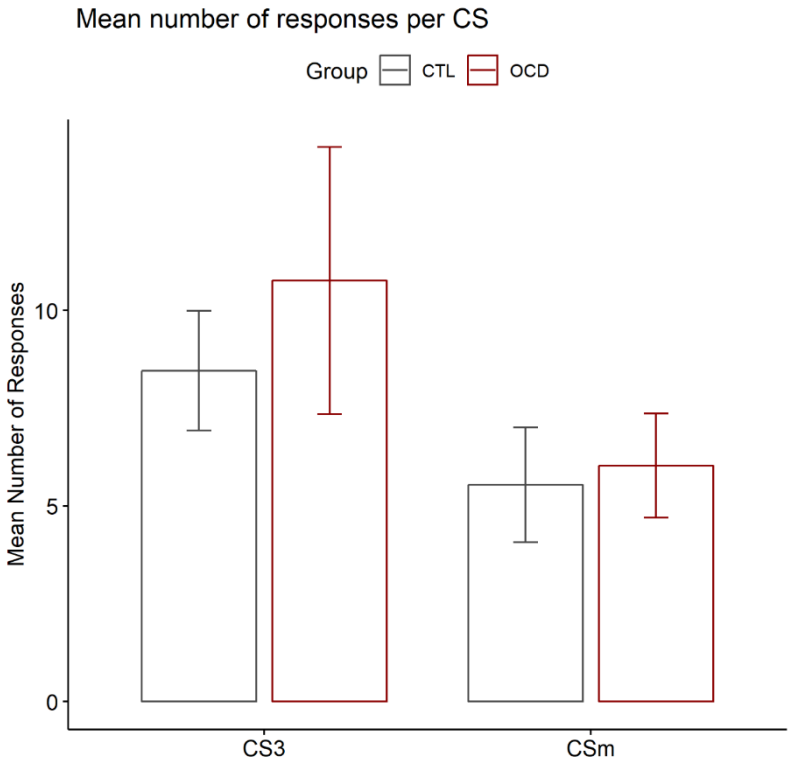

FIGURE 3.10: GENERAL PIT WAS FIRST ASSESSED BY INVESTIGATING THE MEAN NUMBER OF RESPONSES MADE TOWARDS CS3 AND CSM. THERE WAS A SIGNIFICANT EFFECT OF CS, WHERE PARTICIPANTS MADE MORE RESPONSES TO CS3 COMPARED TO CSM (REGARDLESS OF GROUP). THIS REVEALS THAT ALL PARTICIPANTS WERE ABLE TO CONDUCT GENERAL TRANSFER.

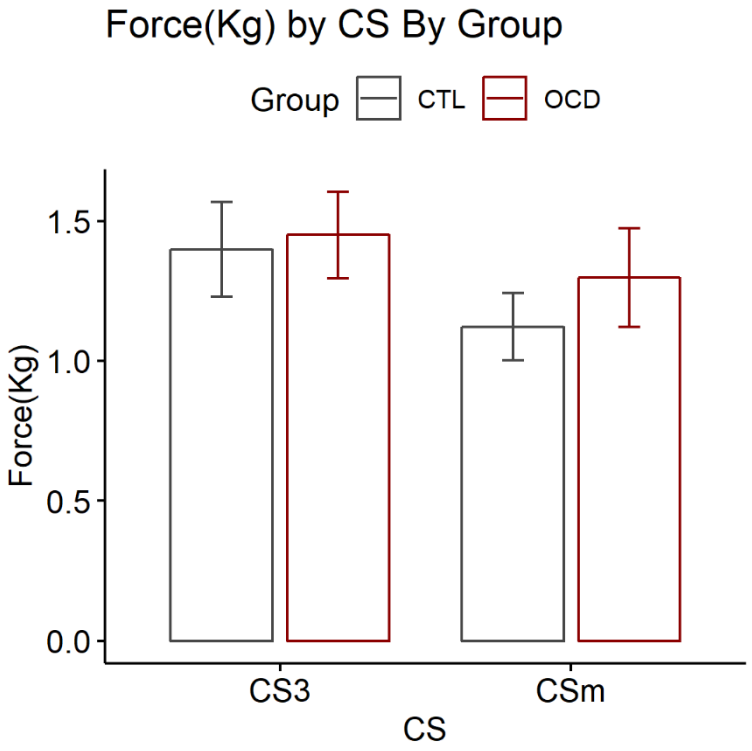

FIGURE 3.11: GENERAL PIT WAS FURTHER ASSESSED BY CHECKING THE AMOUNT OF FORCE APPLIED ON THE HAND DYNAMOMETER WHEN RESPONDING TO CS3 AND CSM. RESULTS SHOWED A TREND (P = .051) FOR

PARTICIPANTS TO APPLY MORE FORCE WHEN RESPONDING TO CS3 COMPARED TO CSM (WITH NO DIFFERENCES BETWEEN GROUP).

Unfortunately, as a result of software issues (in Acqknowledge 3.9) some participants were missing a small proportion of event triggers (that signal the beginning of a new trial) in their force data files. Due to the inter-trial interval being variable, it was not possible to precisely pinpoint when the event triggers were meant to occur, and as a result force responses associated with missing event triggers had to be discarded from the analyses. There was no significant difference in mean number of events removed per participant between groups (CTL: 1.5 ± 2.12; OCD: 1.37 ± 1.86; Wilcoxon rank-sum test: $p = 1.00$). Additionally, there were no noticeable differences in proportion of events missing per CS-type (CS1: .056, CS2: .060, CS3: .043, CSm: .068; $\chi 2(3) = 1.63$; $p = .65$).

3.4.2 Exploratory Medication Analyses

The analyses were repeated dividing OCD into MED- and MED+. This analysis is termed exploratory as the sample size in each group is limited. MED- and MED+ had significantly higher anxiety, depression, and OCD severity scores compared to CTL, but MED- and MED+ were equivalent to each other on all demographic, intelligence, and clinical measures.

Table 3.2: Mean scores and standard deviations per group and statistical test.

	CTL (n = 20)	MED- (n = 8)	MED+ (n = 11)	STATISTIC	PAIRWISE COMPARISONS
GENDER (F:M)	13:7	6:2	6:5	$\chi 2(1) = 0.014$; p = .90	N/A
AGE	15.95 ± 2.05	16.32 ± 1.69	16.27 ± 1.86	F(2,36) = 0.15, p = .86	N/A
WASI-II (IQ)[a]	111.75 ± 10.29	108.75 ± 13.25	108.81 ± 15.03	F(2,36) = 0.60, p = .56	N/A
Digit Span (Forwards)[a]	11.05 ± 2.63	12.0 ± 2.00	10.64 ± 2.66	F(2,36) = 0.70, p = .51	N/A
Digit Span (Backwards)[a]	8.40 ± 2.44	7.63 ± 2.20	8.36 ± 1.63	$\chi 2(2) = 1.75$; p = .42	N/A
BDI**	45.2 ± 6.89	57.5 ± 11.43	60.18 ± 8.33	$\chi 2(2) = 16.12$; p = .00032	MED- & MED+ > CTL MED- = MED+
BAI**	47.85 ± 9.55	68.88 ± 10.71	66.55 ± 10.03	F(2,36) = 29.18, p = 2.93e-08	MED- & MED+ > CTL MED- = MED+
OCI**	8.85 ± 7.13	32.50 ± 17.94	29.00 ± 13.82	F(2,36) = 16.19, p = 9.66e-06	MED- & MED+ > CTL MED- = MED+
CY-BOCS	N/A	24.88 ± 6.24	22.18 ± 4.29	t(17) = 1.12, p = .28	N/A

Key: CTL: Control Group; MED-: Unmedicated patient group; MED+: Medicated patient group; WASI-II: Wecshler's Abbreviated Scale of Intelligence – II; IQ: Intelligence Quotient; BDI: Beck's Depression Inventory (t-scored); BAI: Beck's Anxiety Inventory (t-scored); OCI: Obsessive-Compulsive Inventory; CY-BOCS: Child Yale-Brown Obsessive-Compulsive Scale. *p<.05; **p<.01; [a] missing data from one MED- participant.

Post-hoc tests revealed that compared to CTL, MED+ and MED- had elevated depression (Pairwise Dunn's tests, MED- vs CTL: p = .021, MED+ vs CTL: p = .00072), anxiety (Pairwise t-tests, MED- vs CTL: t(36) = 6.23; p = 1.03e-06, MED+ vs CTL: t(36) = 6.17; p = 1.22e-06), and obsessive-compulsive scores (Pairwise t-tests, MED- vs CTL: t(36) = 4.74; p = .00010, MED+ vs CTL: t(36)

= 4.50; p = .00021). There were no differences on these measures between MED- and MED+ (all p > .05).

Briefly, there was no effect of medication status over all instrumental learning measures, specific transfer, and general transfer (all Group effects were p > .05).

Nonetheless, there were effects of medication present during the Pavlovian phase. When making explicit associations between CSs and USs, 8/8, 7/8, and 8/8 MED- participants answered correctly for CS1, CS2, and CS3 respectively. The number of MED+ participants that answered correctly were as follows, CS1: 8/11, CS2: 9/11, and CS3: 10/11. There was a significant effect of medication status for CS1 accuracy (p = .026), but not for CS2 (p = .52) or CS3 (p = .12). When considering only CS1, MED+ answered less accurately than CTL (p = .041), but there were no differences between MED- and MED+ (p = .23) or between MED- and CTL (p = 1.00).

Moreover, when investigating confidence ratings per CS-US association, there was a significant effect of medication status on confidence ratings ($T_{WJ}(1, 22.21) = 9.64$, p = .0051; $\eta 2G = 0.17$). Post-hoc tests revealed that MED+ (0.82±0.20) had lower confidence ratings overall than CTL (0.96±0.067), Z = 4.02; p = .00018 – see Figure 3.12. There were no significant differences in confidence ratings between MED- (0.88±0.20) and CTL, p = .096, as well as between MED- and MED+, p = .55.

There were no effects of medication detected when exploring CS liking ratings and SCR amplitudes (all Group effects were p > .05).

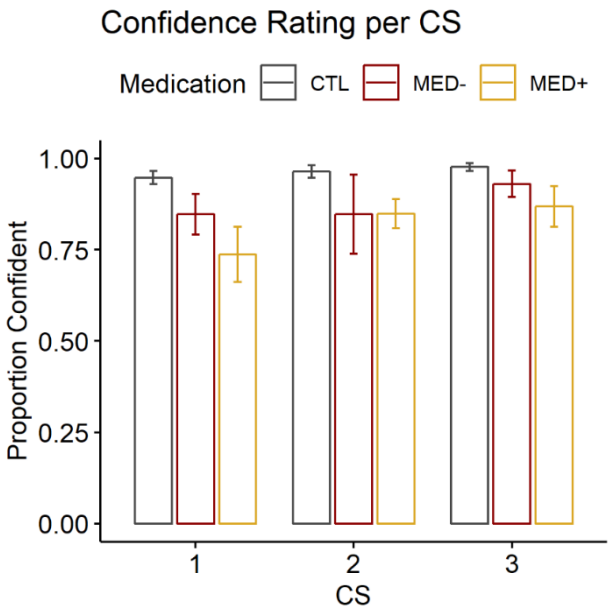

FIGURE 3.12: CONFIDENCE RATINGS PER CS-US ASSOCIATION FROM PAVLOVIAN PHASE. OVERALL, MED+ DISPLAYED LOWER CONFIDENCE COMPARED TO CTL. THERE WERE NO SIGNIFICANT DIFFERENCES IN CONFIDENCE RATINGS BETWEEN MED- AND CTL, AS WELL AS BETWEEN MED- AND MED+.

3.4.3 Correlation Analyses

When considering all participants, there was a significant relationship between verbal memory span (forwards digit span score) and number of responses to CS3 during the PIT phase (r = 0.34, *p* = .033).

When considering only OCD, larger working memory span (backwards digit span score) was associated with less responses to CSm (r =-0.54, *p* = .017), indicative of better general transfer. Next, there initially appeared to be a significant effect of OCD severity: those with higher OCI scores (r = -0.61, *p* =.0056) and higher CY-BOCS scores (r = -0.46, *p* =.046) made fewer responses to CSm. However, age also correlated negatively with this measure (r = -0.57, *p* =.010), as well as showed a significant association with OCI scores (r = 0.53, *p* = .021) and marginally with CY-BOCS scores (r = 0.45, *p* =.054). Hence, I conducted a partial Pearson's correlation analysis between OCD severity and mean responses to CSm whilst controlling for age. OCI scores (*p* = .066) and CY-BOCS (*p* = .26) scores were no longer significantly associated with decreased responses to CSm.

Within MED+, medication dosage significantly correlated with IQ (r = 0.61; *p* =.049).

Finally, there were no significant correlations between task measures and demographic/clinical measures when considering only CTL and only MED-.

3.4.4 Summary of Main Results

CTL and OCD revealed equivalent learning during Instrumental and Pavlovian phases, however OCD were significantly less confident in their CS-US association ratings compared to CTL, which was driven primarily by the MED+ group. Next, CTL and OCD revealed intact specific transfer as both groups made more congruent responses to CSs that previously predicted USs from the instrumental phase. Both groups also displayed intact general transfer as they made more responses to CS3 (aversive stimulus only present in Pavlovian) compared to the neutral CS (CSm). There was also a trend for increased force applied in response to CS3 compared to CSm, which is also indicative of intact general transfer. In sum, there were no significant distinctions between CTL and OCD in strength of specific and general transfer, nor in the number of responses/force applied overall.

3.5 Discussion

In this study, I aimed to probe the effects of aversive Pavlovian cues on instrumental avoidance, as well as indirectly investigate model-based behaviour and harm avoidance, in adolescents with OCD on a recently developed aversive Pavlovian-to-Instrumental Transfer (PIT) paradigm. All adolescents, regardless of OCD presence, revealed intact learning during instrumental and Pavlovian conditioning, and further displayed significant specific and general transfer effects during the PIT phase. Adolescent OCD patients did not show any tendencies for increased avoidance responding during instrumental and PIT phases, and rated their urges to avoid the aversive stimuli as being similar to controls. However, during Pavlovian conditioning, adolescents with OCD, particularly those medicated with SSRIs, had lower confidence in their explicit CS-US ratings. The medicated patients also showed slightly reduced accuracy in their explicit CS-US pairings.

The lack of overall group differences in learning and strength of specific/general transfer appear to contradict previous findings of reduced instrumental and implicit learning in adolescents and children with OCD (Gottwald et al., 2018; Vloet et al., 2010). However, the task employed by Gottwald et al. (2018) was appetitive in nature, whereas the current study employed an aversive PIT paradigm. The aversive contexts present in the task may have motivated the adolescents with OCD to respond congruently during the PIT phase to enable successful avoidance of the unpleasant noises. Hence, it could be that a bias for model-free/habit-directed responding is only present in appetitive contexts where adolescent patients are perhaps less motivated to tap into model-based processes that are more cognitively demanding. Moreover, superior safety learning is found to be associated with traits of

anxiety and compulsivity (Wise & Dolan, 2020), further supporting OCD patients' intact performance during aversive PIT. However, there are caveats to equating specific and general transfer to model-based and model-free processes respectively, which are discussed further on in this section.

Next, patients in my study did not make more avoidance responses nor report higher subjective urges to avoid the aversive stimuli than controls, indicating that punishment sensitivity is not enhanced in these patients with OCD. These results contrast with previous work highlighting loss or punishment aversion in adult patients with OCD (Endrass et al., 2011; Morein-Zamir et al., 2013), as well as subjective ratings of increased harm avoidance in paediatric patients (Bey et al., 2017; Cervin et al., 2020; Ecker & Gönner, 2008; Ettelt et al., 2008). However, emerging computational modelling evidence from probabilistic reversal learning paradigms suggests that adolescent and adult patients with OCD are not affected by punishing feedback (such as losing points) any more than are healthy controls (Hauser et al., 2017; Kanen et al., 2019). It is possible that enhanced harm avoidance in OCD only occurs within a narrow range of circumstances, for example during shock avoidance paradigms (Apergis-Schoute et al., 2017; Gillan et al., 2014) as shocks may be more threatening/painful than aversive auditory stimuli, or when patients' symptoms are directly provoked (Banca, Voon, et al., 2015).

The only significant group difference detected was in confidence ratings of CS-US associations during the Pavlovian phase, where adolescents with OCD overall rated their confidence as being lower. This aligns with meta-memory research reporting reduced memory confidence, but intact memory performance in patients with OCD (Boschen & Vuksanovic, 2007; Hermans et al., 2008; MacDonald et al., 1997; Tolin et al., 2001). However, no studies have directly probed meta-memory in adolescents with OCD except Farrell, Waters, Boschen, and Milliner (2011) who unfortunately did not compare their patients to a control group and hence we cannot infer whether meta-memory is predominantly atypical in juvenile-OCD. Meta-memory research typically employs paradigms that are designed to provoke stress and a sense of responsibility in individuals with OCD. For instance, the 'stovetop task' requires participants to check a virtual or real stovetop several times and to rate their confidence in remembering to check all the necessary knobs, thus simulating a scenario that would commonly trigger compulsive behaviour in individuals with OCD in real-life (Boschen & Vuksanovic, 2007; Coles, Radomsky, & Horng, 2006). The Pavlovian phase in the current PIT paradigm may have also prompted stress in patients with OCD, especially as there was no way to defend themselves against incoming unpleasant noises. In contrast, patients' memory confidence was on par with controls in the instrumental phase possibly due to participants having more control over

the task outcomes, as they were able to prevent the delivery of the unpleasant noises by learning appropriate response-outcome associations.

Similar to Chapter 2, I have detected an effect of medication: medicated patients with OCD were slightly less accurate in matching USs to CSs and also reported the lowest memory confidence out of all groups in the Pavlovian phase. Unfortunately, past studies showing implicit and instrumental learning in youths with OCD did not explore the effects of medication on performance (Gottwald et al., 2018; Vloet et al., 2010) and hence it is uncertain whether SSRIs do in fact play a role in these learning processes. Nevertheless, half of Vloet et al.'s subjects with OCD were medicated with SSRIs (10/20) while most adolescents with OCD in Gottwald et al.'s study were also medicated (23/36), suggesting a possible influence of SSRIs on learning. In addition, as highlighted in the Discussion section of Chapter 2, low dose SSRIs have been found to impair learning and flexibility in healthy participants (Skandali et al., 2018), and indeed in this current chapter SSRI dosage showed a significant positive relationship with IQ. Hence, there is a possibility that lower doses of SSRIs are disrupting learning and memory confidence in medicated patients, although this is speculative as memory confidence during the Pavlovian phase did not correlate with medication dosage.

Moreover, recently Apergis-Schoute et al. (in-prep) found that adults with OCD medicated with SSRIs were more impaired at acquisition learning (learning contingencies prior to a reversal) on a probabilistic reversal learning task compared to medication-naïve patients and control subjects. Authors suggest that the medicated patients may have had a more severe form of OCD to have necessitated psychotropic medication treatment. Similarly, it may be the case in this current, as well as previous, chapter that SSRIs successfully reduced clinician rated symptoms of OCD, which is why medicated and unmedicated patients showed comparable symptom severities, but deficits in cognition and meta-cognition remain especially impaired in the medicated group.

Despite their low confidence, the OCD group were generally able to learn CS-US associations similarly to controls during the Pavlovian phase as indicated by their explicit responses and CS liking ratings (participants' liking ratings for the aversive CSs decreased while their liking of the CSm increased). Unfortunately, SCR results appeared to be uninformative of learning ability as participants' SCR amplitudes showed no significant differentiation between the aversive CS and neutral CS. Instead, on average, CS3 significantly elicited higher SCRs compared to CS2, potentially due to CS3 being associated with a novel US in the Pavlovian phase. Overall, the SCR results may have been the result of equipment issues as previous fear conditioning studies have found that healthy children and adolescents do show appropriate SCR differentiation for neutral and aversive stimuli

(Geller et al., 2017; McGuire et al., 2016; Neumann, Waters, & Westbury, 2008). Although great care had been taken to ensure set-up of SCR apparatus and analyses were being done correctly, signal contamination may still have occurred.

Next, there is an emerging debate surrounding the cognitive processes being employed during specific and general transfer in PIT paradigms. The majority of PIT studies consider specific and general transfer to be a proxy for goal-directed and habit-directed behaviour respectively (Hogarth, Balleine, Corbit, & Killcross, 2013; Hogarth et al., 2019; van Timmeren et al., 2020). However, Garofalo and Robbins (2017) found in their aversive PIT study that outcome devaluation (explicit removal of the object delivering an outcome, in this case removal of headphones delivering unpleasant sounds) failed to decrease both specific and general transfer in healthy participants, suggesting that both types of transfer reflect more habitual responding. Moreover, overtraining, which is commonly considered to enhance habit-directed behaviour (Dayan & Berridge, 2014; Tricomi, Balleine, & O'Doherty, 2009; Yin & Knowlton, 2006) actually increased specific transfer in Garofalo and Robbins' study. Additionally, stronger PIT effects, collapsed across specific and general transfer, have been reported to be negatively associated with model-based reasoning (Sebold et al., 2016). These results suggest that habitual/model-free processes are underlying both specific and general transfer, which may explain why adolescents with OCD were able to conduct both types of transfer similarly to healthy adolescents in my study.

Nonetheless, other studies employing *appetitive* PIT paradigms have demonstrated that outcome devaluation does reduce specific PIT responses in participants (Hogarth et al., 2019; van Timmeren et al., 2020), suggesting that specific PIT under appetitive contexts is goal-directed. Perhaps task valence is key here; in fearful or aversive contexts it may be crucial for safety behaviours to persist and become automatic, leading to such behaviours being present even though the previously aversive environment is now safe. In contrast, continuing to conduct reward-seeking behaviour in neutral environments that were previously appetitive is not as necessary for survival. This underscores why specific transfer responses appeared more habitual in Garofalo and Robbins' (2017) aversive PIT task compared to in aforementioned studies employing appetitive PIT tasks. Research directly comparing the effects of aversive and appetitive PIT on behaviour is necessary to answer these pertinent queries.

3.5.1 Limitations

Regrettably the SCR results were inconclusive, hence I was unable to replicate the finding of abnormal SCR differentiation displayed by paediatric OCD patients as reported by Mcguire et al.

(2016)'s and Geller et al. (2017). Moreover, I was unable to verify from the SCR data whether participants had learnt the US-CS associations during the Pavlovian phase, although fortunately I was still able to confirm successful learning from participants' reports of explicit associations and liking ratings.

Next, due to technical issues, some participants were missing trials in their force data (see Results section), although this did not differ significantly between participant groups and CSs. Nevertheless, the missing data may have contributed to the relatively weaker effect of CS-type (whether CS3 or CSm) on force applied by participants, as Garofalo & Robbins (2017) reported their participants applied significantly more force towards CS3 compared to CS- in their study.

Lastly, the somewhat limited sample, especially when dividing the OCD group by medication status, makes it difficult at this stage to draw strong conclusions. Krypotos and Engelhard (2020) found significant results in their PIT study with 28 subjects in their high OC group, which suggests that slightly larger samples in each of my groups may reveal more prominent effects.

3.5.2 Conclusion

Adolescents with OCD and healthy adolescents alike display intact instrumental and Pavlovian learning, alongside intact specific and general transfer on a novel aversive PIT paradigm. This indicates that adolescents with OCD are able to mobilize goal-directed faculties supposedly necessary to conduct specific transfer, although there is equivocation regarding whether specific transfer is indeed tapping into goal-directed processes. Moreover, there was no difference in frequency of avoidance responding between groups, suggesting that adolescent patients are not excessively harm avoidant. Next, adolescent patients are generally able to correctly learn instrumental and Pavlovian contingencies although medicated patients are slightly less accurate in explicitly pairing CS and US stimuli and also report lower memory confidence. This suggests that SSRI medication may be linked to disrupted implicit learning and reduced meta-memory. However, in spite of this, medicated patients were still able to conduct general and specific transfer to the same extent as other groups. In light of these results, it is clear that adolescents with OCD are generally unimpaired on deterministic tasks such as the PIT task and WCST from Chapter 2. Hence, the remainder of this thesis employs tasks with probabilistic structures (see Chapters 4-6) which better aligns with recent child-OCD research on decision-making and uncertainty.

Chapter 4: Investigating Model-Based Decision-Making in Adolescents with OCD

4.1 Introduction

Researchers typically associate model-based and model-free reasoning with goal-directed and habitual behaviour respectively (Cushman & Morris, 2015; Daw, Niv, & Dayan, 2005; Doya, Samejima, Katagiri, & Kawato, 2002). Behaving in a model-based way is cognitively taxing as it involves building a mental decision-tree comprising all possible states, actions, and outcomes present in an environment (Dolan & Dayan, 2013). Model-based learners use this cognitive map to constantly 'plan ahead' in order to make optimal decisions, which requires a degree of goal-directed control. In contrast, model-free behaviour is less cognitively demanding as decision-making is based on prediction errors or most recent feedback instead of planning (Dolan & Dayan, 2013). Model-free individuals learn from the immediate outcomes garnered after sampling choices; if the outcome gained is equivalent to what was predicted, an individual will continue applying the same strategy. If outcome and prediction differ, strategies are updated accordingly. Habitual responding, which simply involves continuously responding in the same way or to the same stimulus, is a characteristic strategy of model-based behaviour as it is a computationally efficient way of making decisions, albeit at the cost of behavioural flexibility (Cushman & Morris, 2015).

Research has demonstrated an imbalance between goal-directed and habitual control in individuals with OCD (Gillan & Robbins, 2014). Outcome devaluation tasks have been instrumental in highlighting this imbalance. Adults with OCD are more prone to responding to devalued stimuli (Gillan et al., 2014, 2011; Snorrason, Lee, de Wit, & Woods, 2016), suggestive of a reliance on more habitual strategies. Adolescents with OCD also display poor goal-directed control; an outcome devaluation study found they were worse at responding to valuable trials and withholding their responses to devalued trials (Gottwald et al., 2018). Moreover, paediatric patients display poor goal-directed planning highlighted by their tendency to be slower and require more moves on planning tasks such as the TOL and SOC (Huyser et al., 2010; Kim et al., 2018; Ornstein et al., 2010). In fact, impaired goal-directed planning has been found in adult and child patients, as well as their first-degree relatives (Bey et al., 2018; Cavedini et al., 2010; Delorme et al., 2007; Negreiros et al., 2019; Vaghi, Hampshire, et al., 2017), making it a candidate cognitive endophenotype and thus a robust feature of OCD. Moreover, prefrontal and striatal brain areas thought to underlie goal-directed and habitual control typically show aberrant activity in children and adults with OCD (Banca, Voon, et

al., 2015; Bernstein et al., 2016; Gilbert et al., 2009; Gillan & Robbins, 2014; Vaghi, Vértes, et al., 2017).

In neurotypical adults, model-free and model-based signatures of behaviour are thought to operate in parallel, and often compete for control (Daw et al., 2011). Studies have directly probed this using a two-stage decision task, considered to be a gold standard task for delineating model-free from model-based behaviour. The two-stage decision task also shows construct validity with outcome devaluation paradigms (Friedel et al., 2014), demonstrating that model-free and model-based behaviours are related to goal-directed and habitual control. In brief, the task involves participants navigating from a first stage to a second stage to gain rewards (see Methods section of this chapter for visualisation of this task). In Stage 1, there are two stimuli participants can choose from, one with a higher probability of transitioning to a state with one pair of stimuli, while the other has a higher probability of transitioning to a state with a different pair of stimuli. When in one of the these new states (which forms Stage 2), participants have to choose one of the stimuli to receive rewards. The probabilities of the four Stage 2 choices providing rewarding feedback changes slowly and independently through a random Gaussian walk process. The extent of a subject's model-based learning can be determined through observing their Stage 1 choices. A model-based learner would take into account transition probabilities (from Stage 1 to Stage 2), wherein they would make Stage 1 decisions based on which Stage 2 state they are aiming to transition into (i.e. to the Stage 2 state that has a stimulus that offers more rewards at the time). In contrast, a model-free learner is more likely to make Stage 1 decisions based purely on which choice led to a rewarding outcome in the preceding trial. Adults with OCD reveal more model-free behaviour on the task than healthy controls, making choices based on which stimulus most recently offered rewards rather than attending to and making inferences from the task structure (Voon, Baek, et al., 2015; Voon, Derbyshire, et al., 2015; Wheaton et al., 2019). Additionally, dimensional psychiatry studies reveal that more model-free behaviour on the task is associated with increased compulsivity in healthy individuals (Gillan et al., 2019; Gillan, Kosinski, Whelan, Phelps, & Daw, 2016). All in all, these results suggest that adults with OCD rely more on model-free strategies to make decisions over model-based ones.

Hitherto, research has not formally captured whether youths with OCD have reduced model-based control compared to typically developing adolescents. Model-based behaviour in healthy people has been found to emerge with age, as it is absent in children, increasingly present during adolescence, and finally strengthened in adulthood (Decker, Otto, Daw, & Hartley, 2016). However, a recent study has obtained evidence for model-based strategies being utilised even by young children; in an adapted two-step decision-making task, where trials were either high stake (value of rewards were 5-fold) or

low-stake (value of rewards were 1-fold), children as young as 5 years old were able to employ mostly model-based strategies when stakes were higher (Smid, Kool, Hauser, & Steinbeis, 2020). Intriguingly and most relevant to juvenile-OCD, development of model-based control is found to be reduced in adolescents who have had high compulsivity traits from a young age (Vaghi et al., 2020) which suggests that symptoms of OCD disrupt healthy maturation of model-based behaviour (Loosen & Hauser, 2020).

4.1.1 Reinforcement Learning-Drift Diffusion Model

Nearly all studies employing the two-step decision-making task computationally model their data using a reinforcement learning model (first conceptualised by Daw et al., 2011) in order to derive estimates of model-based behaviour. In this model, the choices participants make at each stage of the task are used to estimate the model-based *w* parameter. High values of *w* indicate more model-based behaviour and *vice versa*. Additionally, likelihoods of choices are estimated using a softmax logistic function containing an inverse temperature parameter, but this method has been criticised for failing to capture the dynamics of decision-making. The inverse temperature parameter represents the extent to which subjects partake in value-driven over exploratory decision-making, but value-driven decision-making in itself is a complex process and the parameter is not informative of underlying factors contributing to a bias for either type of choosing.

Recently, computational psychiatry work is utilising a class of models known as drift-diffusion models (DDM) (Ratcliff & Rouder, 1998) to supplement existing reinforcement learning (RL) models and overcome the limitations of using a softmax choice rule. DDM aims to capture noisy processes leading up to a decision and it assumes that choices are made by continuously sampling noisy decision evidence until a decision boundary is reached in favour of one of two alternatives (Forstmann, Ratcliff, & Wagenmakers, 2016). This is done by modelling reaction times alongside choice data, enabling more detailed understanding of latent decision-making processes. Reinforcement learning studies have thus opted to combine standard RL models with DDM (leading to a new class of models termed RL-DDM) to reap the benefits of both types of models (Fontanesi, Gluth, Spektor, & Rieskamp, 2019; Pedersen, Frank, & Biele, 2017). A major benefit to using RL-DDM is that it can be used to capture various factors contributing to decision-making, not just limited to feedback sensitivity and tendencies for exploitation/exploration, but also evidence accumulation efficiency and the trade-off between speed versus accuracy during response selection (Pedersen et al., 2017). In particular, RL-DDM can further disentangle processes contributing to value-driven decision-making which is only captured by the inverse temperature parameter in standard RL models. For instance, parameters embedded in the RL-DDM can address whether a tendency for choosing

the more valuable option stems from clear and accurate representations of all choice values, favouring accurate over speedy decision-making, or from a tendency to favour exploitative over exploratory decision-making (Pedersen et al., 2017). In the context of model-based/model-free decision-making, Shahar et al. (2019) reported that fitting a RL-DDM to two-step decision-making task data led to more reliable estimates of the model-based *w* parameter. Moreover, parameters from the DDM portion of the model enabled better understanding of model-based decision-making. The drift rate scaling parameter (see Statistical Analyses section of this chapter for more details), which captures the extent to which subjects are able to discriminate between values associated with competing choices, correlated with model-based *w* values as well as predicted increased advantageous choice selection and quicker response times. This highlights that being able to discriminate effectively between choice values is indicative of greater model-based control.

Drift-diffusion models applied to perceptual decision-making tasks have been particularly informative in highlighting inefficient evidence accumulation in OCD: child and adult patients show reduced drift rate parameter values compared to healthy population (Banca, Vestergaard, et al., 2015; Erhan et al., 2017; Mandali et al., 2019) indicative of poor information processing and less perceptual discrimination between competing choices (Voss, Rothermund, & Voss, 2004). In addition, patients show increased evidence accumulation and slower responding (indexed by a decision boundary parameter from DDM) when uncertainty is high but despite this increased cautiousness, patients do not make more accurate choices compared to controls, which is again suggestive of poor evidence processing (Banca, Vestergaard, et al., 2015; Erhan et al., 2017; Mandali et al., 2019). Cautious decision-making without performance improvement has also been found in paediatric patients on goal-directed planning tasks (Kim et al., 2018; Ornstein et al., 2010). Collectively, these findings denote disrupted evidence accumulation to be the reason for impaired decision-making in OCD. In addition, as efficient evidence accumulation (measured via drift rates) is associated with model-based behaviour in the sequential decision-making task (Shahar et al., 2019), it is likely that poor model-based control in OCD is also linked to patients' disrupted evidence accumulation.

Therefore, in this current study I modelled two-step decision-making task data obtained from adolescents with OCD and healthy adolescents using a RL-DDM previously implemented by Shahar et al. (2019) in an effort to decompose several latent decision-making processes and explore how they link to model-based behaviour. Concretely, I sought to understand 1) whether model-based decision-making is indeed reduced in adolescents with OCD compared to healthy controls, if so 2) what are the decision-making processes contributing to this reduced model-basedness, and 3) are these processes alone abnormal in adolescents with OCD? Using parameters from RL-DDM I was

able to consider various factors contributing to reduced model-based behaviour and disrupted decision making, namely feedback sensitivity, a bias for exploratory/exploitative decision-making, maladaptive choice perseveration, poor information processing/value discrimination, and reduced speed of evidence accumulation. Additionally, using the RL-DDM which accounts for both choices and response times enabled more reliable and holistic estimates of model-based behaviour (Shahar et al., 2019). In line with prior work on adults with OCD, I hypothesised that adolescents with OCD would show reduced model-based decision-making on this task possibly linked to impaired evidence accumulation.

4.2 Methods

4.2.1 Sample

Forty-one participants were recruited to complete the Sequential Decision Making task, however data for one control participant failed to be saved due to software issues. Thus, in total, 40 participants (20 OCD, 20 CTL) completed the task. Eleven patients with OCD were receiving SSRI medication at the time of completing the task, while 9 patients were medication-naïve. Out of the 11 medicated patients, 8 were receiving sertraline while 3 were receiving fluoxetine. Mean SSRI dosage was 97.27 mg (s.d. 58.33) and the dose ranged from 20 mg to 200 mg. Digit span and IQ data is unavailable for one participant with OCD. Further demographic details are outlined in the Results section of this chapter.

4.2.2 Sequential Decision-Making Task

This task was originally used by (Decker et al., 2016) and was adapted from Daw et al.'s (2011) Two-Step Markov Decision-Making task. The task was designed to distinguish between model-free and model-based decision-making strategies. This particular version was created with a child-friendly narrative and colourful imagery, designed to be engaging to young participants.

Task

Each trial in the task consisted of two choice stages (see Figure 4.1). In the first stage, participants chose between two spaceships; Choosing the blue spaceship had a 70% probability of transitioning to the red planet (common transition) and a 30% probability of transitioning to the purple planet (rare transition). Choosing the green spaceship was associated with opposite transition probabilities (30% red and 70% purple). Based on their Stage 1 choices, participants would either transition to the red

or purple planet, forming Stage 2. In Stage 2, there were two aliens on each planet, and participants had to choose one of the aliens to uncover possible treasure. After choosing an alien, participants would either be presented with a picture of treasure or nothing, according to a slowly drifting probability between 0.2 and 0.8. This gradual changing reward-probability was to encourage exploration of choices. Participants had 3 seconds (s) in Stage 1 and Stage 2 to respond, otherwise the current trial would terminate and move on to the following trial. Following choices in Stage 2 was 1s of animation, 1s of reward feedback, and a 1s inter-trial interval. The task consisted of 200 trials separated into 4 blocks.

At the end of the task, to ascertain knowledge of the task structure, participants were asked to select the spaceship that mostly went to the red planet.

Tutorial

Participants underwent an extensive tutorial to ensure they understood the task before moving on to the experimental phase. They were first introduced to the alien stimuli and were told that aliens were willing to share treasure with them. However, all aliens need to dig up mines to find treasure, and aliens with a good mine will provide more treasure compared to aliens with a bad mine. Furthermore, an alien with a good mine for now may not necessarily have a good mine later on, and *vice versa* for aliens with bad mines. This was to introduce participants to the idea that the probability of receiving rewards changes slowly between aliens. A series of interactive exercises was presented alongside instructions to ensure participants understood the concepts.

Participants were then introduced to the spaceships, which form Stage 1 of the task. Participants were not made aware of the explicit transition probabilities associated with each spaceship, but were simply told that each spaceship goes to one planet more than the other. A practice round of 20 trials was conducted using aliens and planets that were different from the stimuli presented in the actual experimental phase of the task. After the practice, participants were given hints to further cement their understanding of the task:

Hint 1

Remember which aliens have treasure. How good a mine is changes slowly so an alien that has a lot of treasure to share now, will probably be able to share a lot in the near future

Hint 2

Remember, each alien has its own mine. Just because one alien has a bad mine and can't share very often, does not mean another has a good mine. Also, there are no funny patterns in how an alien shares (treasure) like every other time you ask or depending on which spaceship you took. The aliens are not trying to trick you.

Hint 3

The spaceship you choose is important because often an alien on one planet may be better than the ones on another planet. You can find more treasure by finding the spaceship that is most likely to take you to right planet.

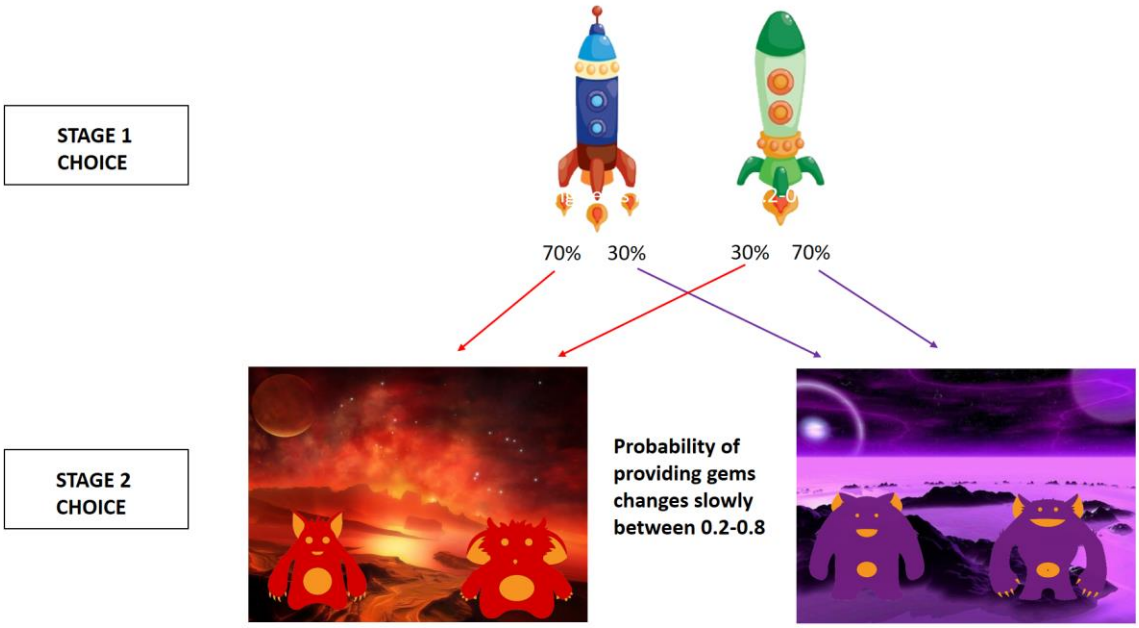

FIGURE 4.1: STRUCTURE OF SEQUENTIAL DECISION-MAKING TASK.

The task was presented using Psychtoolbox-3 and Matlab R2017b.

4.3 Statistical Analyses

4.3.1 Standard Analyses

Data cleaning and statistical analyses were implemented in Matlab R2017b and RStudio 3.5.0.

Mixed regressions were used to analyse task data using the lme4 package (Bates, Maechler, Bolker, & Walker, 2014) implemented in R. Model-based behaviour was assessed using separate models for choices and response times. The first 9 trials per subject were excluded from the analyses, as was

done by Decker et al. (2016). Trials in which subjects failed to make a first- or second-stage choice in time were also removed.

A logistic mixed-effects regression model (previously done by Daw et al., 2011; Decker et al., 2016; Otto et al., 2013) was used to model first-stage choices (stay or switch to stimulus chosen on previous trial) as a function of the Stage 2 outcome from the previous trial (rewarded or not), the previous trial's transition type (common or rare), and an interaction between the two. The rationale behind this regression model is that a purely model-free learner would ignore the last transition and rely primarily on previous outcome to make choices. If the previous trial was rewarded, model-free learners would be more likely to choose the same Stage 1 stimulus regardless of type of last transition. This translates to a significant main effect of the outcome variable in the regression model. Inversely, a model-based subject would have intact knowledge of transition structures and would hence only choose the same stimulus as the previous trial if the trial was rewarded and the last transition type was common. This would manifest as a significant outcome-by-last-transition interaction. To assess how experimental groups (OCD vs CTL) differ in their strategies to the task, group was added to the outcome-by-transition-type interaction term. Per subject variance to the fixed intercept and to the outcome-by-transition-type interaction term were added as random variables (see Equation 4.1).

$$p(Y_{stay(t+1)}) \sim \text{Last-Transition}_t \times \text{Outcome}_t \times \text{Group}_t + (\text{Transition-Type}_t \times \text{Outcome}_t \mid \text{Subject})$$

– Equation 4.1

Probability of repeating Stage 1 choices was plotted as a function of Outcome and Transition-type. A model-free learner's data would be similar to the idealised 'Model-Free' plot in Figure 4.2 and likewise, a model-based learner's data would be similar to the idealised 'Model-Based' plot in the same figure.

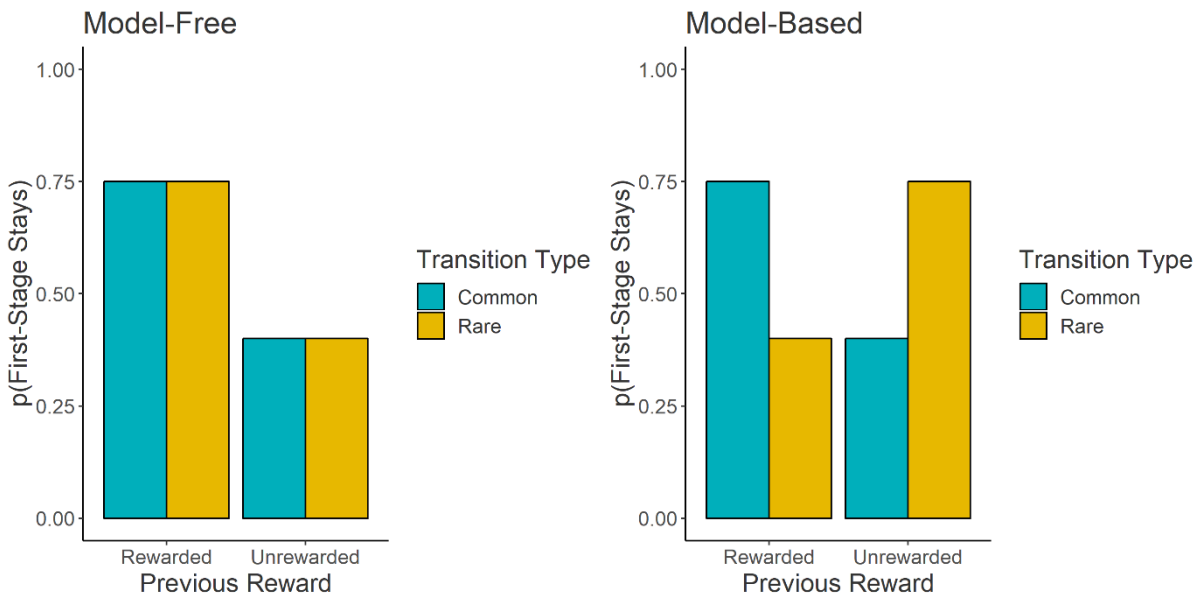

FIGURE 4.2: THE IDEALISED MODEL-FREE LEARNER (LEFT) WOULD SHOW A MAIN EFFECT OF PREVIOUS OUTCOME/REWARD BUT NOT TRANSITION-TYPE, WHILE THE IDEALISED MODEL-BASED LEARNER (RIGHT) WOULD SHOW A SIGNIFICANT OUTCOME-BY-TRANSITION-TYPE INTERACTION.

Next, a linear mixed effects regression was used to model reaction times for Stage 2 choices. Current transition type (common, rare), Group, and an interaction between the two were added as independent variables (see Equation 4.2). Per subject variance to the fixed intercept and to the Current Transition term were added as random variables. Here, it was theorised that model-based learners would slow down Stage 2 responses following rare transitions and speed up following common transitions (show a significant effect of Current Transition), indicating that they had successfully learnt the task structure.

$$RT_{2,t} \sim \text{Current Transition-Type}_t \times \text{Group}_t + (\text{Current Transition-Type}_t \mid \text{Subject}) \quad \text{– Equation 4.2}$$

Per subject beta coefficients/regression slopes associated with the Outcome-by-Last-Transition interaction term (termed MB-I_{Choice}) from the choice regression model, and beta coefficients associated with the Current Transition term (termed MB-II_{RT}) from the response time regression model were extracted as measures of strength of model-based decision-making. Pearson's correlations were conducted between clinical/demographic/intelligence scores and beta coefficients and computational model parameter values (described on next page).

These analyses were then repeated controlling for age and IQ, as model-based reasoning has been found to strengthen with age (Decker et al., 2016) and is associated with higher order thinking skills (Otto, A. R., Skatova, A., Madlon-Kay, S., & Daw, 2015; Otto, Raio, Chiang, Phelps, & Daw, 2013). The analyses were also repeated with the OCD group divided into medicated (MED+) and

unmedicated (MED-) groups to assess the effects of SSRI treatment on model-based ability in adolescent OCD.

4.3.2 Reinforcement Learning Models

The full reinforcement learning model for this task has been described in detail in prior studies (Daw et al., 2011). At each trial (t), the model takes into account the three states present in the task: Stage 1 with rockets represented by $s_{1,t}$, the planet experienced in Stage 2 represented by $s_{2,t}$, and the planet not experienced represented by $s_{3,t}$, as well as the actions (stimulus chosen) taken at each state (a_1 for Stage 1 and a_2 for Stage 1). The value of each Stage 1 choice stimulus (Q) at each trial is determined via the sum of two components: 1) the model-free value (Q_{MF}) that reflects the previous trial's outcome (rewarded or not) in Stage 2 after choosing a specific stimulus in Stage 1 (i.e. the Q_{MF} value for a chosen Stage 1 stimulus would increase if the previous Stage 2 outcome is rewarding) and 2) the model-based value (Q_{MB}) that reflects the highest value out of the two stimuli in Stage 1, which is in turn based on whether a specific chosen stimuli is associated with a common transition towards a rewarding Stage 2 state (e.g. if the red planet in Stage 2 is more rewarding than the purple planet, Q_{MB} would be equal to the Q value of the blue rocket in Stage 1, as it has a higher probability of flying to the red planet when selected). In simpler terms, the model-free component takes into account Stage 2 reward history, while the model-based component takes into account both reward history and transition-type.

In the model, the Stage 2 Q_{MF} was updated using a SARSA(λ) temporal difference learning model (Rummery and Niranjan, 1994):

$$Q_{MF}(s_{2,t+1}, a_{2,t+1}) = Q_{MF}(s_{2,t}, a_{2,t}) + \alpha_2 \delta_{rew,t} \quad \text{– Equation 4.3}$$

Where the reward prediction error, $\delta_{rew,t}$, is defined by the the Stage 2 Q_{MF} subtracted from the Stage 2 outcome, r_t:

$$\delta_{rew,t} = r_t - Q_{MF}(s_{2,t}, a_{2,t}) \quad \text{– Equation 4.4}$$

r_t is 1 when a reward is received, and 0 otherwise.

Next, the Stage 1 Q_{MF} value was updated using both the reward prediction error and state prediction error ($\delta_{state,t}$):

$$Q_{MF}(s_{1,t+1}, a_{1,t+1}) = Q_{MF}(s_{1,t}, a_{1,t}) + \alpha_1 \delta_{state,t} + \alpha_1 \lambda \delta_{rew,t} \quad \text{– Equation 4.5}$$

The state prediction error was defined as the difference in Q_{MF} values between Stage 2 and Stage 1:

$\delta_{state,t} = Q_{MF}(s_{2,t}, a_{2,t}) - Q_{MF}(s_{1,t}, a_{1,t})$ – Equation 4.6

An eligibility trace parameter (λ) (Sutton and Barto, 1998) was used to reduce the influence of the reward prediction error, $\delta_{rew,t}$, on the updating of Stage 1 Q_{MF} values. When λ = 1, both state and reward prediction errors are used to update the current Stage 1 choice value, but when λ = 0, only the state prediction error is taken into account. It is thought that a model-free learner would have high λ values which means that Stage 1 choices which led to rewards in Stage 2 were more likely to be repeated regardless of whether a common or rare transition preceded the reward (Daw et al., 2011).

α in Equations 4.3 and 4.5 is a learning rate parameter used to control how quickly values of Q_{MF} change according to prediction errors, $\delta_{i,t}$. In the full model, there are separate α (α_1 and α_2) for each stage to account for possible differences in learning between the two stages.

As for model-based calculations, the temporal difference learning algorithm calculated the Stage 1 action value (Q_{MB}) for each choice based on the transition probabilities that would lead to the Stage 2 outcome: $P(s_2|a_1) = 0.7$ and $P(s_3|a_1) = 0.3$ for when choice 1 was chosen and $P(s_2|a_1) = 0.3$ and $P(s_3|a_1) = 0.7$ when choice 2 was chosen. The Stage 2 action values in this model-based approach are equivalent to model-free algorithm described above, as the Q-value here is just an estimate based on the immediate reward r_t with no further stages to anticipate. Hence $Q_{MB} = Q_{MF}$ at Stage 2.

The Q_{MB} in Stage 1 for each action, a, at Stage 1 was defined using Bellman's equation as follows:

$Q_{MB}(a_{j,t}) = P(s_2|a_1)*\max[Q_{MF}(s_{2,t})] + P(s_3|a_1)*\max[Q_{MF}(s_{3,t})]$ –Equation 4.7

Here, the transition probabilities for each state were multiplied by the maximum Q_{MF} value of the Stage 2 state visited in that trial.

To connect Q-values to actual participant choices, net action values at Stage 1 were first defined as the weighted sum of the model-free and model-based values:

$Q_{net}(s_1,a_j) = wQ_{MB} + (1-w)\, Q_{MF}(s_1,a_j)$ – Equation 4.8

w is a free floating weighting parameter used to describe the extent of model-based decision making. *w* = 0 indicates pure model-free behaviour while w = 1 indicates pure model-based behaviour. The probability of a choice in Stage 1 is then calculated using a softmax function involving the value of Q_{net}:

$$p(a_{1,t} = a|s_{1,t}) = \frac{\exp(\beta_1[Q_{net}(S_{1,t},a_{1,t})+p.rep(a_{1,t})])}{\sum_{a'} \exp(\beta_1[Q_{net}(S_{1,t},a_{1,t}')+p.rep(a_{1,t}')])}$$ – Equation 4.9

While the probability of a choice in Stage 2 was calculated using another softmax function but this time involving Q_{MF}:

$$p(a_{2,t} = a|s_{2,t}) = \frac{\exp(\beta_2[Q_{MF}(s_{2,t},a_{2,t})])}{\sum_{a'} \exp(\beta_2[Q_{MF}(s_{2,t},a_{2,t}')])}$$ – Equation 4.9

The free inverse temperature parameter β_i controls the extent to which options in each stage were chosen according to their Q_{net} values. High values of β_i indicate more reward maximisation/exploitation while lower values reflect decision-making inconsistent with choice values (more exploration). β_i was allowed to vary between stages in the full model ($\beta_1$and β_2). This was done to capture any possible differences in choice-value consistency between stages. The function rep(a) is a binary indicator, equating to 1 if the choice in the current trial (a_t) matched the choice in the previous trial (a_{t-1}). Free parameter p described the tendency to make perseverative choices during the first stage, wherein higher values signify increasing perseveration. p was not included in the softmax function for Stage 2 choices as different states are visited from trial to trial and hence choice repetition is less likely to play a role in behaviour.

In this full model, 7 free parameters were included: β1, β2, α1, α2, λ, p, and w. The full model was compared with a model that contained a single β and α for both stages, to assess whether this simpler model with 5 parameters was better able to capture participant behaviour than the full model.

In addition, a model was formulated to assess whether behaviour was better explained by algorithms with separate learning rates for rewarding (point gained) and neutral (no point gained) outcomes. A similar TD learning model with separate learning rates has been implemented in a study exploring risky decision-making in healthy adolescents (Rosenbaum, Grassie, & Hartley, 2020). The particular model for this study was identical to the full reinforcement learning model described above, except the learning rate in the TD algorithm would be represented by α_{rew} if the Stage 2 outcome was rewarding ($r_t = 1$), and α_{neu} if no reward was received ($r_t = 0$). This is how Stage 2 Q_{MF} would be updated:

$$Q_{MF}(s_{2,t},a_{i,t}) = Q_{MF}(s_{i,t},a_{i,t}) + \alpha_{rew,i}\delta_{rew,t} - \text{ if } r_t = 1$$ – Equation 4.10

$$Q_{MF}(s_{2,t},a_{i,t}) = Q_{MF}(s_{i,t},a_{i,t}) + \alpha_{neu,i}\delta_{rew,t} - \text{ if } r_t = 0$$ – Equation 4.11

The valence-based learning rates were also used when updating the Stage 1 Q_{TD} using the Stage 2 prediction error:

$$Q_{MF}(s_{1,t},a_{1,t}) = Q_{MF}(s_{1,t},a_{1,t}) + \alpha_{rew}\delta_{state,t} + \alpha_{rew}\lambda\delta_{2,t} -$$ if $r_t = 1$ – Equation 4.12

$Q_{MF}(s_{1,t},a_{1,t}) = Q_{MF}(s_{1,t},a_{1,t}) + \alpha_{neu}\delta_{state,t} + \alpha_{neu}\lambda\delta_{2,t} -$ if $r_t = 0$ – Equation 4.13

Two versions of models with α_{rew} and α_{neu} parameters were assessed: one with β allowed to vary between stages, and one with a single β. In total, 4 RL models were fitted to data and compared.

4.3.3 Reinforcement Learning + Drift Diffusion Model

To better capture the dynamics of decision-making processes and take into account choice latencies, I programmed a reinforcement learning drift diffusion model (RL-DDM), similar to the one implemented by Shahar et al. (2019). The basic DDM assumes that decisions are made by continuously sampling noisy decision evidence until a decision boundary in favour of one of two alternatives is reached. This particular model is termed a Wiener drift diffusion model whereby the decision process is described as a continuous random walk process.

In RL-DDM, evidence was accumulated to one of two boundaries at each stage on every trial, with the two boundaries representing choice 1 and choice 2 respectively. Time taken to reach either one of the boundaries on either trial as well as the distance between the two boundaries determined the response time and choice. At each trial, the RL-DDM calculates the likelihood of the RT of choice *i* with the Wiener first passage of time (WFPT) distribution:

$RT_{s,i,t} \sim$ WFPT $[a, T, z, v(t)]$ – Equation 4.14

Where the WFPT returns the probability that choice *i* was chosen along with the observed RT. The distribution contains four parameters, the first one being the boundary separation parameter (*a*). This parameter adjusts the speed-accuracy trade-off, and describes the amount of evidence needed until a decision boundary is reached. Higher values of *a* reflect more evidence accumulated leading to more careful, slower, and more accurate decisions. A smaller *a*, inversely, indicates faster and more erratic decisions.

Next, the non-decision time parameter (*T*) adjusts the time used on processes not related to decision-making, including stimulus encoding and motor processes. Tasks with higher motor complexity tend to elicit greater values of *T* (Voss et al., 2004).

The starting point parameter (*z*) controls the extent to which one choice is preferred over another before decision evidence is available.

Lastly, the drift rate parameter (*v*) describes 'perceptual sensitivity' (Voss et al., 2004), indicating how quickly evidence from choices can be processed. A high *v* indicates higher sensitivity to the differences in value between different choices, leading to quicker and accurate choices. In contrast,

a lower *v* represents less discriminability between choice values leading to higher likelihood of 'guessing'.

As *v* reflects value sensitivity, it was mathematically defined as the difference in values between choice 1 and choice 2 at each stage multiplied by the scaling parameter, *m*. For Stage 1, the differences between $Q_{net}(2)$ and $Q_{net}(1)$ was used:

$v_{s,t} = m * [Q_{net,t}(2) - Q_{net,t}(1)]$ – Equation 4.15

Meanwhile, the difference between Q_{MF} for choice 1 and choice 2 was used to define drift rates on Stage 2:

$v_{s,t} = m * [Q_{MF,t}(2) - Q_{MF,t}(1)]$ – Equation 4.16

The free parameter *m* transforms the difference between Q values to an appropriate scale for the DDM framework. As *m* is proportional to *v*, higher values of *m* translated to greater drift rates. In other words, when *m* is 1 (the lowest possible value) the drift rates, *v*, are equal to the simple difference between Q values. But as *m* increases, even small differences between Q-values are magnified and this results in faster decisions towards the choice with the greater Q-value.

a, *T*, and *m* were free parameters in the model. *z* was fixed to be 0.5 as I assumed no prior bias towards either choice (as was done in Shahar et al.'s study). Separate *a*, *T*, and *m* parameters were used for Stage 1 and Stage 2 (Shahar et al., 2019). The WFPT distribution replaced the softmax function from the standard reinforcement learning model. Parameters from the winning standard RL model were included in the RL-DDM model alongside the DDM parameters.

4.3.4 Model-Fitting

Hierarchical Bayesian inference was used for model-fitting, wherein the mean and variance for each model parameter was drawn from a group level distribution separate for OCD and CTL groups. The method described here was similar to that used in Chapter 2. Group level parameters (indicated by the notation $_{group}$) were sampled from the following priors below. Prior distributions used for DDM parameters here were the same ones used in Pedersen et al. (2017).

$\alpha 1_{group}, \alpha 2_{group}, \alpha_{group}, \alpha_{rew,\,group}, \alpha_{neu,\,group}, \lambda_{group}, p_{group}, w_{group}, T_{group} \sim \text{Uniform}\ (0,1)$

$\beta_{group}, \beta 1_{group}, \beta 2_{group} \sim \text{Uniform}\ (0,10)$

$a 1_{group}, a 2_{group} \sim \text{Uniform}\ (1,3)$

$m_{group} \sim$ Uniform (1,10)

Next, inter-subject variability, σ, in the model parameters were sampled from the priors below. Variability priors for parameters from the standard RL model were taken from Kanen et al. (2019) while variability priors for parameters from the RLDDM model were taken from Perdersen et al. (2017).

$\sigma_{\alpha 1}, \sigma_{\alpha 2}, \sigma_{\alpha}, \sigma_{\alpha rew}, \sigma_{\alpha neu}, \sigma_{\lambda}, \sigma_{p}, \sigma_{w} \sim$ Half-normal (0,0.05)

$\sigma_{\beta 1}, \sigma_{\beta 2} \sim$ Half-normal (0,1)

$\sigma_{a1}, \sigma_{a2}, \sigma_{T1}, \sigma_{T2}, \sigma_{m1}, \sigma_{m2} \sim$ Uniform (0.001, 5)

Subject-level trial-by-trial parameters were each represented by a Gaussian prior distribution, with the mean and standard deviations of the distributions sampled from respective group level distributions. For example, $\alpha_{subject} \sim$ Normal ($\alpha_{group}, \sigma_{\alpha}$).

Computation of the posteriors were conducted via MCMC sampling using JAGS software (Plummer, 2003). Four randomly initialised MCMC chains were run during model-fitting. I used the JAGS Wiener module (Wabersich & Vandekerckhove, 2014) containing the aforementioned WFPT distribution to estimate the likelihood of RTs and choices. Model comparison was conducted by calculating the Deviance Information Criterion (DIC) which takes into account accuracy of model fit and penalises model complexity (number of free parameters) enabling prevention of over-parameterisation (Wilson & Collins, 2019). Lower DIC values indicate better fit.

Posterior distributions were interpreted using the 95% HDI. Comparisons between patients and controls were calculated by subtracting the posterior distributions of the control group-parameters from the posterior distributions of the patient group-parameters, generating the group mean differences per parameter. The 95% HDIs of the posterior distribution for the group mean differences were calculated and inspected to check whether they reliably included zero (indicating no difference between groups).

To assess effects of SSRI treatment on decision-making and model-based behaviour computational modelling analyses were repeated with the OCD group divided into MED- and MED+.

4.3.5 Parameter Recovery

Parameter recovery was conducted to verify the validity of the winning model and that parameter values were meaningful (and not occurring by chance) (Wilson & Collins, 2019). The winning RL

and RL-DDM models were first used to simulate synthetic data from 100 ‘participants’ each in the CTL and OCD groups. Simulation was conducted in Matlab R2017b. Code for parameter recovery was adapted from Shahar et al. (2019). The free parameters were replaced with the mean fitted parameter values per group estimated from the actual human data. I then ascertained whether the true parameter values could be recovered by fitting the winning model to the simulated data, and checking whether the true and generated parameter values fell within their corresponding 95% HDI. This same method for parameter recovery was conducted by Apergis-Schoute et al. (in-prep).

4.4 Results

4.4.1 Standard Results (CTL vs OCD)

Demographic, clinical, and intelligence scores are summarised in Table 4.1. OCD and CTL were matched for age, gender, and IQ. There were also no differences in digit span scores. OCD displayed significantly increased depression, anxiety, and obsessive-compulsive scores.

Table 4.1: Mean Scores and standard deviations per group and measure.

	CTL (n = 20)	**OCD (n = 20)**	**STATISTIC**
GENDER (F:M)	13/7	13/7	N/A
AGE	16.20 ± 1.98	16.32 ± 1.69	Z = 0.12; p= .90
WASI-II (IQ)[a]	112.35 ± 10.89	107.63 ± 13.96	t(37) = 1.18; *p*=.25
BDI**	44.55 ± 7.22	58.55 ± 9.56	Z = -4.07; *p*= 4.62e-05
BAI**	47.40 ± 5.82	67.20 ± 9.93	Z =-5.09; *p* = 3.57e-07
OCI**	8.10 ± 6.67	30.70 ± 14.94	t(26.30) = -6.20 ; *p* = 1.48e-06
CY-BOCS	N/A	23.32 ± 5.22	N/A
Digit Span (Forwards)[a]	10.80 ± 2.86	8.30 ± 2.20	Z = -0.23, *p* = .82
Digit Span (Backwards)[a]	11.21 ± 2.44	8.05 ± 1.87	*t*(37) = 0.38, *p* =.71

Key: CTL: Control Group; OCD: Obsessive-Compulsive Disorder group; WASI-II: Wecshler's Abbreviated Scale of Intelligence – II; IQ: Intelligence Quotient; BDI: Beck's Depression Inventory (t-scored); BAI: Beck's Anxiety Inventory (t-scored); OCI: Obsessive-Compulsive Inventory; CY-BOCS: Child Yale-Brown Obsessive-Compulsive Scale. *p<.05; **p<.01; [a] missing data from one OCD participant.

All participants except for 1 CTL subject were able to correctly identify the Stage 1 rockets that most likely went to each Stage 2 planet, indicating that majority of participants (and importantly, all OCD subjects) successfully learnt the probabilities associated with Stage 1 choices.

The results of the mixed effects logistic regression for first-stage stays revealed a significant effect of Outcome, as well as a significant Outcome-by-Transition-Type interaction. In other words,

participants repeated choices when the most recent previous choice resulted in a reward. They also repeated choices when the previous choice was followed by a common transition that resulted in a reward. There was no main effect of Group (CTL vs OCD) or any significant interactions with this variable. The results are summarised in Table 4.2 and Figure 4.3.

Table 4.2: Results of Mixed Logistic Regression on First-Stage Stays

Fixed Effects	**Beta Coefficient**	**Standard Error**	**Z-Value**	**p-value**
Outcome (win)**	0.37	0.054	6.81	9.82e-12
Last Transition (Common)	0.050	0.049	1.01	.31
Group	0.17	0.11	1.47	.14
Outcome x Last Transition **	0.45	0.085	5.30	1.17e-07
Outcome x Group	0.080	0.051	1.75	.081
Last Transition x Group	0.030	0.046	0.66	.51
Outcome x Last Transition x Group	0.073	0.083	0.87	.38

*p<.05; **p<.01

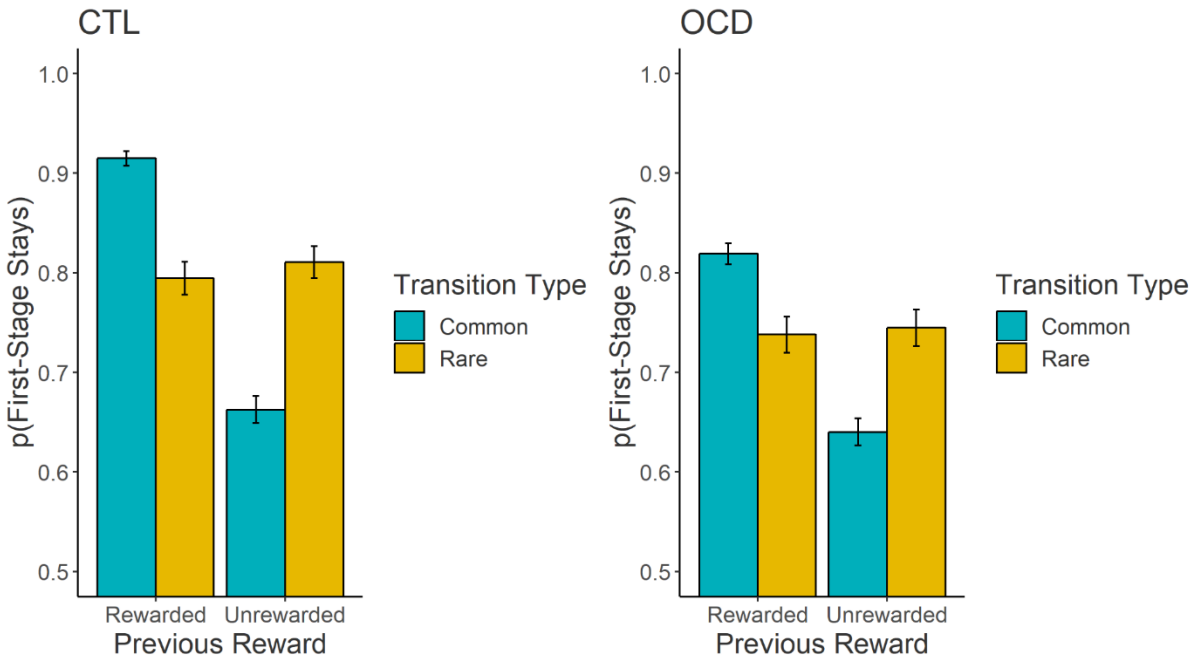

FIGURE 4.3: PROPORTION OF FIRST STAGE STAYS PLOTTED BY TRANSITION TYPE (COMMON VS RARE), BY PREVIOUS REWARD (REWARDED VS UNREWARDED) AND BY GROUP (CTL VS OCD). REGRESSION ANALYSES SHOWED NO DIFFERENCES BETWEEN GROUPS IN EFFECTS OF TRANSITION TYPE AND PREVIOUS OUTCOME ON FIRST STAGE STAYS. FIRST STAGE STAYS, FOR ALL PARTICIPANTS, WERE MORE LIKELY TO OCCUR FOLLOWING REWARDED TRIALS (MODEL-FREE BEHAVIOUR) AND FOLLOWING TRIALS WHICH WERE REWARDED DURING COMMON TRANSITIONS (MODEL-BASED BEHAVIOUR). HENCE, PARTICIPANTS TENDED TO DISPLAY A MIXTURE OF MODEL-FREE AND MODEL-BASED BEHAVIOUR.

The regression analysis was repeated this time adding z-scored age and IQ scores as interaction terms (see Table 4.3). There was a main effect of IQ, suggesting participants with higher IQ repeated Stage 1 choices more than those with lower IQ. IQ also showed a significant positive interaction with Outcome-by-Last-Transition, indicating that participants with higher IQ were more likely to make model-based choices.

Table 4.3: Results of Mixed Logistic Regression on First-Stage Stays with IQ and Age as interaction terms

Fixed Effects	Beta Coefficient	Standard Error	Z-Value	P-Value
Outcome	0.76	0.49	1.55	0.12
Last Transition	-0.37	0.44	-0.83	0.41
Group	0.097	0.11	0.90	0.37
Age	0.062	0.10	0.60	0.55
IQ*	0.017	0.0087	1.96	0.050
Outcome x Last Transition **	-2.21	0.62	-3.59	0.00033
Outcome x Group	0.096	0.055	1.75	0.080
Last Transition x Group	0.020	0.049	0.42	0.68
Outcome x Last Transition x Group	0.0053	0.069	0.076	0.94
Outcome x Age	-0.022	0.052	-0.41	0.68
Last Transition x Age	-0.049	0.047	-1.04	0.30
Outcome x Last Transition x Age	0.026	0.066	0.40	0.69
Outcome x IQ	-0.0036	0.0045	-0.80	0.42

Last Transition x IQ	0.0038	0.0040	0.94	0.35
Outcome x Last Transition x IQ**	0.024	0.0056	4.33	1.51e-05

*p<.05; **p<.01

Next, the linear mixed effects regression on Stage 2 response times showed a significant effect of Current Transition (see Table 4.4 and Figure 4.4), wherein rare transitions resulted in slower response times. There was no significant effect of Group.

Table 4.3: Results of Linear Mixed Regression on Second-Stage Response Times

Fixed Effects	**Beta Coefficient**	**Standard Error**	**t-value**	**df**	**p-value**
Current Transition (rare)**	-0.077	0.011	-6.95	37.66	2.98e-08
Group	0.025	0.021	1.22	38.01	0.23
Current Transition x Group	-0.018	0.011	-1.61	37.66	0.12

*p<.05; **p<.01

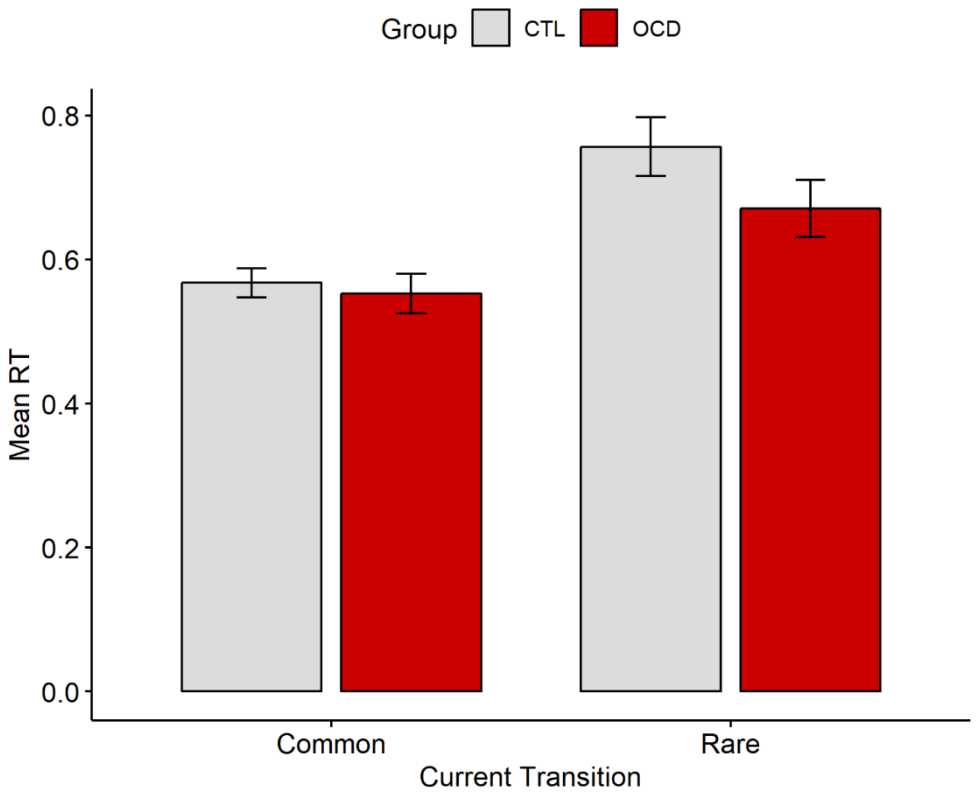

FIGURE 4.4: RESPONSE TIMES WERE SLOWER FOLLOWING RARE TRANSITIONS COMPARED TO COMMON TRANSITIONS, INDICATING THAT PARTICIPANTS HAD INTACT KNOWLEDGE OF TRANSITION PROBABILITIES ASSOCIATED WITH EACH FIRST-STAGE CHOICE. THERE WERE NO DISTINCTIONS BETWEEN OCD AND CTL.

The response-time regression analyses were repeated controlling for age and IQ (see Table 4.5). There was a significant interaction between Current Transition and IQ. In other words, those with higher IQ displayed slower reaction times when current transitions were rare, indicating superior model-based knowledge of transitions in participants with higher IQ.

Table 4.5: Results of Linear Mixed Regression on Second-Stage Response Times with Age and IQ as Interaction Terms

Fixed Effects	Beta Coefficient	Standard Error	T-Value	Df	P-Value
Current Transition	0.18	0.095	1.88	34.53	0.069
Group	0.023	0.021	1.07	35.01	0.29
Age	0.0019	0.021	0.091	35.01	0.93
IQ	0.0025	0.0017	1.42	35.00	0.16
Current Transition x Group	-0.010	0.011	-0.96	34.61	0.35
Current Transition x Age	0.0054	0.010	0.52	34.60	0.61
Current Transition x IQ **	-0.0023	0.00086	-2.72	34.56	0.01

*p<.05; **p<.01

4.4.2 Exploratory Medication Analyses

Next, the analyses were repeated dividing the OCD group into MED- and MED+. Demographic, intelligence, and clinical scores are found in Table 4.6.

Table 4.6: Mean Scores and standard deviations per group and measure.

	CTL (n = 20)	MED- (n = 9)	MED+ (n=11)	STATISTIC	PAIRWISE COMPARISONS
GENDER (F:M)	13/7	7/2	6/5	$X^2(2) = 1.17$, p= .56	N/A
AGE	16.20 ± 1.98	16.37 ± 1.58	16.29 ± 1.86	$X^2(2) = 0.099$, p= .95	N/A
WASI-II (IQ)[a]	112.35 ± 10.89	108.75 ± 13.25	106.82 ± 15.03	$F(2,37) = 0.73$; p = 0.49	N/A
BDI**	44.55 ± 7.22	56.56 ± 11.06	60.18 ± 8.33	$X^2(2) = 17.06$, p= .00020	MED- & MED+ > CTL MED- = MED+
BAI**	47.40 ± 5.82	68.0 ± 10.36	66.55 ± 10.03	$F(2,37) = 29.00$; p = 2.65e-08	MED- & MED+ > CTL MED- = MED+
OCI-R**	8.10 ± 6.67	32.78 ± 16.80	29.00 ± 13.82	$F(2,37) = 19.11$; p = 1.99e-06	MED- & MED+ > CTL MED- = MED+
Y-BOCS	N/A	24.88 ± 6.24	22.18 ± 4.29	$t(17) = 1.12$, p = .28	N/A
Digit Span (forwards)[a]	10.80 ± 2.86	12.0 ± 2.00	10.64 ± 2.66	$F(2,36) = 0.73$; p = .49	N/A
Digit Span (backwards)[a]	11.21 ± 2.44	7.63 ± 2.20	8.36 ± 1.63	$F(2,36) = 0.37$; p = 0.69	N/A

Key: CTL: Control Group; MED-: Unmedicated patient group; MED+: Medicated patient group WASI-II: Wechsler's Abbreviated Scale of Intelligence – II; IQ: Intelligence Quotient; BDI: Beck's Depression Inventory (t-scored); BAI: Beck's Anxiety Inventory (t-scored); OCI: Obsessive-Compulsive Inventory; CY-BOCS: Child Yale-Brown Obsessive-Compulsive Scale. *p<.05; **p<.01; [a] missing data from one OCD participant.

Post-hoc tests revealed that compared to CTL, MED+ and MED- groups had elevated depression (Dunn's test, MED- vs CTL: p = .016, MED+ vs CTL: p = .00043), anxiety (Pairwise t-tests, MED- vs CTL: t(37) = 6.23, p = 9.08e-07, MED+ vs CTL: t(37) = 6.20, p = 1.02e-06), and obsessive-compulsive scores (Pairwise t-tests, MED- vs CTL: t(37) =5.28, p = 1.77e-05, MED+ vs CTL: t(37) =4.78, p = 8.25e-05). There were no differences on these measures between MED- and MED+ (all p = 1.00).

When conducting the logistic mixed regression, there was no significant effect of Medication status on first-stage stays or any significant interactions with the group terms (see Table 4.7). There was also no effect of Medication status on second-stage reaction times (see Table 4.8). As there were no significant effects of group, the analyses were not repeated controlling for age and IQ.

Table 4.7: Results of Mixed Logistic Regression on First-Stage Stays (By Medication Status)

Fixed Effects	Beta Coefficient	Standard Error	Z-Value	P-Value
Outcome**	0.34	0.057	5.91	3.50e-09
Last Transition	0.035	0.051	0.68	.50
MED+	0.22	0.15	1.4	.16
MED-	-0.026	0.18	-0.14	.89
Outcome x Last Transition**	0.42	0.090	0.47	2.48e-06
Outcome x MED+	0.12	0.069	1.74	.082
Last Transition x MED+	0.046	0.061	0.75	.46

Outcome x Last Transition x MED+	0.10	0.11	0.91	.36
Outcome x MED-	-0.053	0.083	-0.65	.52
Last Transition x MED-	-0.094	0.073	-1.30	.20
Outcome x Last Transition x MED-	-0.13	0.13	-0.95	.34

*p<.05; **p<.01

Table 4.8: Results of Linear Mixed Regression on Second-Stage Response Times

Fixed Effects	Beta Coefficient	Standard Error	T-Value	Df	P-Value
Current Transition **	-0.071	0.012	-5.97	36.68	6.94e-07
MED+	0.034	0.018	1.20	37.0	.24
Current Transition x MED+	-0.024	0.015	-1.59	36.67	.12
MED-	-0.017	0.034	-0.50	36.99	.62
Current Transition x MED-	0.013	0.018	0.70	36.59	.49

*p<.05; **p<.01

4.4.3 Computational Modelling Results

Standard Reinforcement Learning

The best-fitting model (as determined by calculating the DIC score) was the model with separate learning rates for rewarding and neutral outcomes, as well as separate inverse temperature parameters for Stage 1 and Stage 2 (see Table 4.9).

Table 4.9: DIC scores per model. Model 3 was the winning model

Model	Parameters	DIC
1	β1, β2, α1, α2, λ (Lambda), p, w	16112.11
2	β, α, λ, p, w	16121.39
3	β1, β2, α_{rew}, α_{neu}, λ, p, w	16079.39
4	β, α_{rew}, α_{neu}, λ, p, w	16097.22

When analysing group differences in model parameter values between OCD and CTL, OCD showed lower Stage 2 inverse temperature values (β2) compared to CTL indicating an increased tendency for exploration (less value-driven responding) during Stage 2, but no group differences were detected on other parameters including the model-based *w* parameter (see Figure 4.5).

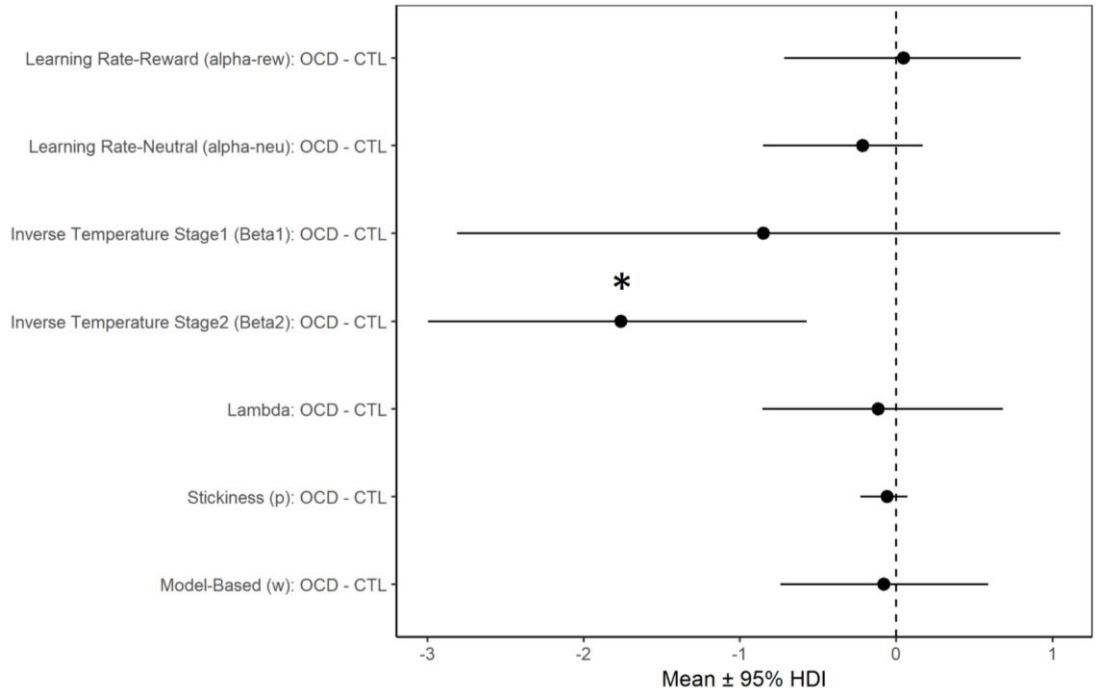

FIGURE 4.5: SUMMARY OF GROUP DIFFERENCES PER PARAMETER FROM THE BEST-FIT COMPUTATIONAL MODEL. ERROR BARS REPRESENT THE HIGHEST DENSITY INTERVALS (HDI) OF THE POSTERIOR DISTRIBUTIONS OF GROUP

DIFFERENCES (OCD-CTL) IN GROUP MEAN PARAMETER VALUES. THE GROUP DIFFERENCE HDI FOR B2 (BETA2) WAS NEGATIVE AND DID NOT INCLUDE 0, INDICATING THAT OCD HAD LOWER B2 VALUES THAN CTL.

When dividing the OCD group by medication status and re-fitting the winning model to data, it was found that MED+ had lower β2 values compared to CTL (see Figure 4.6), indicating the aforementioned effect of OCD was driven by MED+. There were no groups differences on other parameters.

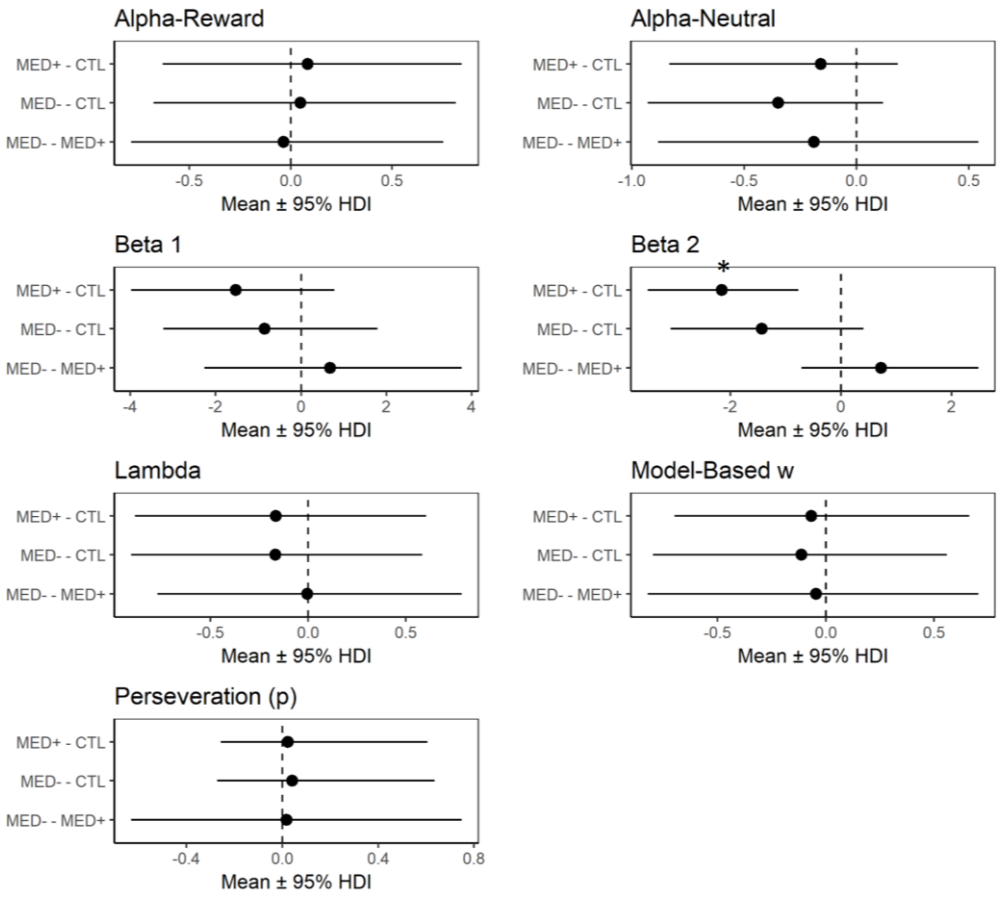

FIGURE 4.6: SUMMARY OF GROUP DIFFERENCES (CTL VS MED- VS MED+) PER PARAMETER FROM THE BEST-FIT COMPUTATIONAL MODEL. EACH PLOT REPRESENTS GROUP MEAN DIFFERENCE RESULTS FOR EACH MODEL PARAMETER. ERROR BARS REPRESENT THE HIGHEST DENSITY INTERVALS (HDI) OF THE POSTERIOR DISTRIBUTIONS OF GROUP DIFFERENCES IN GROUP MEAN PARAMETER VALUES. MED+ WAS FOUND TO HAVE LOWER B2 VALUES COMPARED TO CTL.

Reinforcement Learning + Drift Diffusion Model

The winning RL model was included as the RL portion of the RL-DDM, excluding the softmax function and inverse temperature parameters. In total, the RL-DDM had 11 free parameters, similar

to the model implemented by Shahar et al. (2019). The parameters are α_{rew}, α_{neu}, λ, p, w, *a*1, *a*2, *T*1, *T*2, *m*1, *m*2.

After fitting the model to data and calculating group mean differences, it was found that OCD had a markedly lower boundary separation parameter value for Stage 2 (*a*2) compared to CTL, indicative of less careful evidence accumulation, and favouring speed over accuracy. There were no distinctions between groups for other parameters (see Figure 4.7).

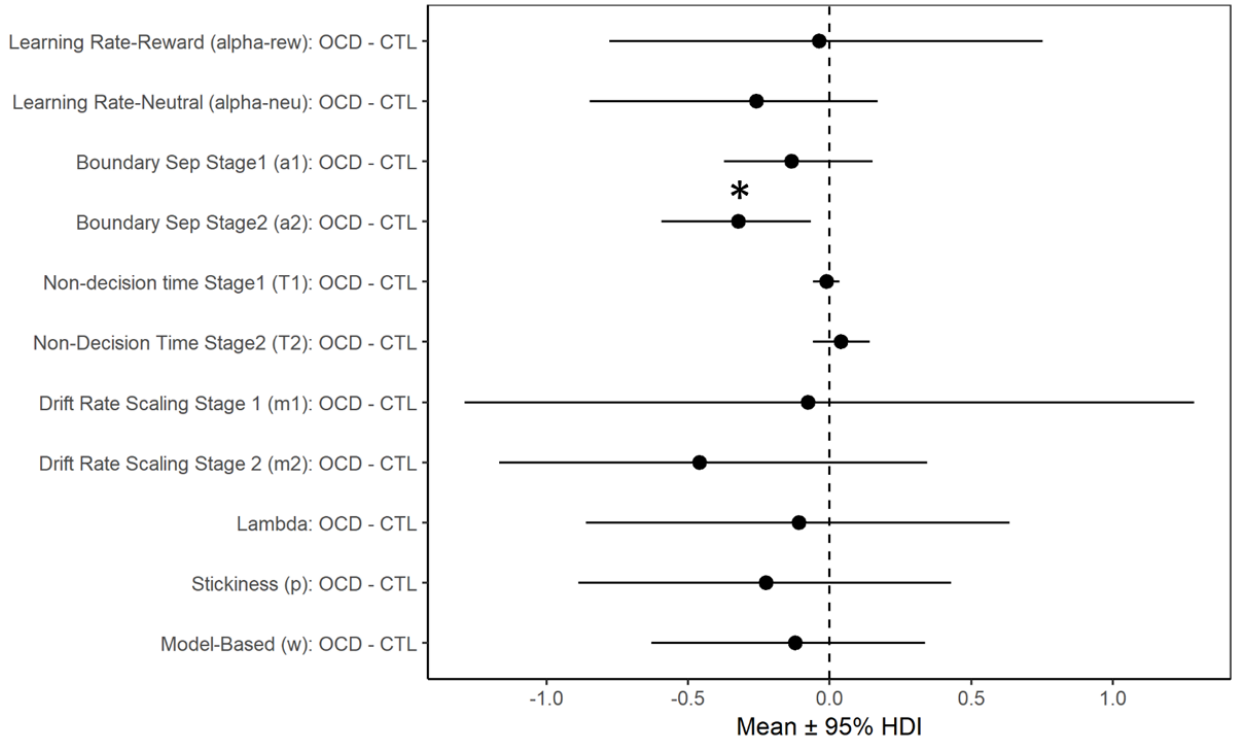

FIGURE 4.7: SUMMARY OF GROUP DIFFERENCES PER PARAMETER FROM THE RL-DDM COMPUTATIONAL MODEL. ERROR BARS REPRESENT THE HIGHEST DENSITY INTERVALS (HDI) OF THE POSTERIOR DISTRIBUTIONS OF GROUP DIFFERENCES (OCD-CTL) IN GROUP MEAN PARAMETER VALUES. OCD DISPLAYED LOWER A2 VALUES THAN CTL.

In addition, the same RL-DDM but with separate group parameters for MED- and MED+ was fit to data. Group mean difference analyses revealed lower *a*2 parameter values for MED+ compared to CTL (see Figure 4.8). MED- and MED+, as well as MED- and CTL were equivalent on this parameter. Although, MED- showed credibly lower *a*2 values than CTL when considering mean 90% HDI. No other group differences on other parameters were detected.

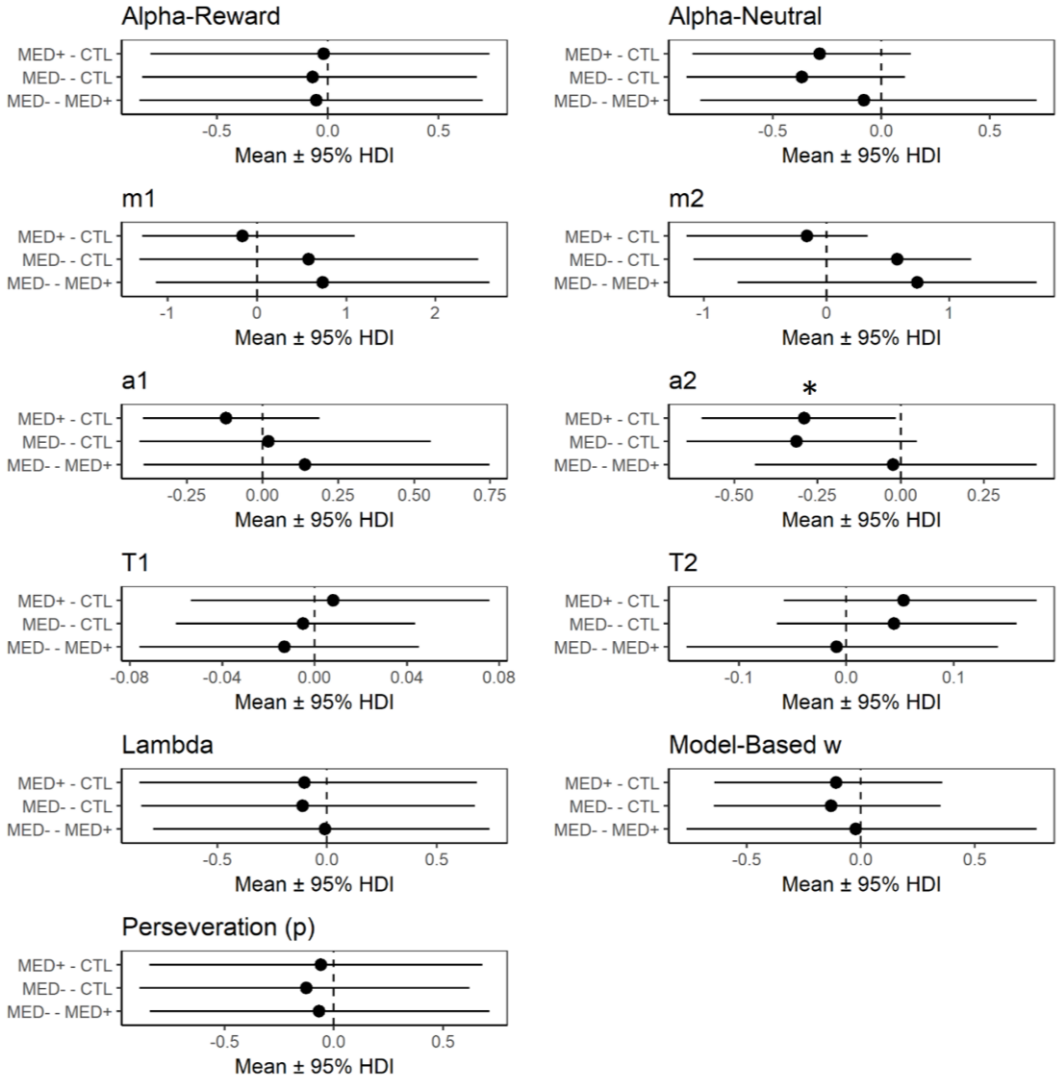

FIGURE 4.8: SUMMARY OF GROUP DIFFERENCES (CTL VS MED- VS MED+) PER PARAMETER FROM THE BEST-FIT COMPUTATIONAL MODEL. EACH PLOT REPRESENTS GROUP MEAN DIFFERENCE RESULTS FOR EACH MODEL PARAMETER. ERROR BARS REPRESENT THE HIGHEST DENSITY INTERVALS (HDI) OF THE POSTERIOR DISTRIBUTIONS OF GROUP DIFFERENCES IN GROUP MEAN PARAMETER VALUES. MED+ WAS FOUND TO HAVE LOWER A2 VALUES COMPARED TO CTL (95% HDI). NOT PICTURED: MED- SHOWED LOWER A2 VALUES WHEN CALCULATING THE MEAN 90% HDI.

Parameter Recovery

Previously-fitted parameters used to generate the simulated data and their corresponding recovered values are presented in Table 4.10 for the RL model and Table 4.11 for RL-DDM. All generative parameter values fell strictly within their corresponding recovered 95% highest posterior density intervals (HDI) indicating successful parameter recovery.

Table 4.10: Parameter recovery analysis with simulated data generated by best-fit reinforcement learning model

Group	**Parameter**	**Empirical values**	**Simulated values**	**95% HDI Interval**
CTL	α-rew	0.44	0.44	[0.41, 0.47]
	α-neu	0.91	0.91	[0.88, 0.95]
	β1	4.94	4.97	[4.79. 5.19]
	β2	4.61	4.56	[4.34, 4.80]
	λ	0.66	0.68	[0.64, 0.72]
	p	0.24	2.34	[0.22, 0.25]
	w	0.60	0.60	[0.58, 0.63]
OCD	α-rew	0.49	0.50	[0.47, 0.53]
	α-neu	0.69	0.67	[0.65, 0.70]
	β1	4.09	4.05	[3.85, 4.25]
	β2	2.84	2.80	[2.69, 2.91]
	λ	0.54	0.51	[0.48, 0.55]
	p	0.18	0.17	[0.16, 0.18]
	w	0.52	0.50	[0.47, 0.53]

Table 4.11: Parameter recovery analysis with simulated data generated by best-fit reinforcement learning drift diffusion model

Group	**Parameter**	**Empirical values**	**Simulated values**	**95% HDI Interval**
CTL	α-rew	0.53	0.53	[0.52, 0.56]
	α-neu	0.90	0.94	[0.90, 1.00]
	*a*1	1.31	1.32	[1.30, 1.33]
	*a*2	1.58	1.59	[1.58, 1.60]
	*m*1	1.75	1.66	[1.58, 1.75]
	*m*2	1.88	1.86	[1.80, 1.91]
	T1	0.025	0.026	[0.024, 0.028]
	T2	0.036	0.036	[0.035, 0.038]
	λ	0.64	0.67	[0.59, 0.75]
	p	0.48	0.51	[0.48, 0.54]
	w	0.66	0.66	[0.61,0.70]
OCD	α-rew	0.49	0.49	[0.47, 0.52]
	α-neu	0.64	0.67	[0.63, 0.71]
	*a*1	1.18	1.18	[1.17, 1.18]
	*a*2	1.26	1.28	[1.27, 1.29]
	*m*1	1.68	1.59	[1.46, 1.71]
	*m*2	1.42	1.40	[1.34, 1.45]

T1	0.015	0.016	[0.015, 0.017]
T2	0.076	0.077	[0.075, 0.078]
λ	0.53	0.57	[0.52,0.65]
p	0.26	0.26	[0.24, 0.29]
w	0.54	0.55	[0.49, 0.61]

4.4.4 Correlation Analyses

Correlations between clinical symptoms and task measures

When considering all participants, anxiety (r = -0.39, p = .019) and obsessive-compulsive scores (OCI) (r = -0.33, p = .040) were associated with lower β2 values, indicating more exploration in Stage 2. As OCI and anxiety scores also correlated with each other (r =0.80; p <.0001), I re-analysed these correlations partialling out the effects of each independent variable (e.g. checking relationship between OCI and β2 values controlling for anxiety). I found no significant effects of OCI or anxiety on β2 values when doing these partial correlations (all p > .05), suggesting a shared effect of OCI and anxiety on β2 values. Next, still within all participants, high OCI scores were associated with decreased lambda (λ) values (r = -0.31, p =.048) indicating Stage 1 choices were less influenced by Stage 2 rewards. Within only CTL, depression scores were significantly correlated with drift rate scaling values in Stage 1 (m1) (r = 0.49, p = .027), β1 (r = 0.59, p = .0064), and MB-I_{Choice} (r =0.52, p = .019) values.

There were no significant correlations between clinical scores and task measures when considering only OCD, only MED-, and only MED+.

Correlations between age, IQ, working memory and task measures

When considering all participants, IQ correlated with β2 values (r = 0.35, p = .030), and with m1 (r = 0.55, p = .00031) and Stage 2 (m2) (r = 0.39, p = .015). IQ was also predictive of more model-based behaviour as indexed by beta-coefficients obtained from the choice (MB-I_{Choice}) (r = 0.54, p = .00034) and RT (MB-II_{RT}) (r = -0.40, p = .019) mixed regressions. In addition, working memory (measured via backwards digit span scores) correlated with β2 values (r = 0.47, p = .0026), m1 values

(r = 0.41, *p* = .0089), *m*2 values (r =0.53, *p* = .00049), and model-based behaviour indexed by MB-II_{RT} (r =-0.35, *p* =.029). Lastly, older participants displayed increased *m*2 parameter values (r = 0.36, *p* = .022).

Next, within OCD, IQ correlated with several measures, being associated with increased *m*1 (r = 0.67, *p* = .0017), *m*2 (r = 0.49, *p* = .034), lambda (r = -0.47, *p* = .041), β1 (r = 0.66, *p* = .0020), β2 (r = 0.59, *p* = .0076) values and more model-based behaviour indexed by MB-I_{Choice} (r = 0.65, *p* = .0024) and MB-II_{RT} (r = -0.53, *p* = .019). Age also showed a positive association with β2 values (r = 0.54, *p* = .014). Working memory correlated with m1 (r = 0.54, *p* = .016), m2 (r = 0.59, *p* = .0081), and β2 (r = 0.53, *p* = .019) values.

Within CTL, participants with higher IQ showed increased β1 scores (r = 0.53, *p* = .017), while participants with greater working memory span displayed increased perseveration (p) parameter (r = 0.46, *p* = .043) and β2 values (r = 0.46, *p* = .043).

Within MED-, IQ significantly correlated with decreased lambda values (r= -0.89; *p* = .0040), and increased β1 (r= 0.75; *p* = .032) and β2 values (r= 0.77; *p* = .027).

Within MED+, IQ significantly predicted increased β1 (r =0.58, *p* = .018), MB-I_{Choice} (r =0.59, *p* =.012), and reduced MB-II_{RT} (r =-0.75, *p* = .030) values.

Correlations with Medication Dosage

Medication dosage was significantly associated with increased IQ (r =0.61, p =.049), increased m1 values (r =0.62, p = .040), increased reward rates (α-rew) (r =0.70, p = .016), and more model-based behaviour based on MB-II_{RT} (r =-0.75, p =.0077). When partialling out IQ (as it correlated with medication dosage as well as with several task and model measures), only medication dosage's relationship with reward rates remained significant (r =0.80, p = .0055, all other correlations p >.05).

Extra Correlations

In addition, I sought to understand whether increased exploration (shown by decreased β2 values) in OCD was linked to their decreased *a*2 values, as both parameters describe value-based decision-making in Stage 2. In other words, I wanted to check whether increased exploration was linked to patients' tendencies to value speed over accuracy. There was no correlation between the two parameter values within the OCD group (*p* = .79) suggesting values in one were not being driven by the other. Instead β1 and β2 values were significantly influenced by *m*1 (r = 0.78; *p* <.0001) and *m*2 (r = 0.83; *p* < .0001) values respectively, indicating that patients were more likely to choose options

with higher values (more exploitation) when they were able to discriminate effectively between differing choice values. *a*2 values did not correlate with any model parameters.

Correlations between model-based measures and computational model parameters

Finally, to understand how latent decision-making processes relate to model-based behaviour, further correlational analyses were conducted between model-based indices (MB-I_{Choice}, MB-II_{RT}, *w* parameter) and model parameter values (see Table 4.12).

Table 4.12: Correlations between model-based metrics and computational model parameter values

All Participants	MB-I_{Choice}	MB-II_{RT}	*w* - parameter
α-rew	r = 0.41 *p* = .0089	r = -0.42 *p* = .006247	n.s
α-neu	n.s.	n.s	n.s
*m*1	r = 0.71 *p* = 3.63e-07	r = -0.58 *p* = 7.99e-05	n.s
*m*2	r = 0.35 *p* = .026	n.s.	r = 0.40 *p* = .011
T1	n.s	n.s	n.s
T2	n.s	n.s	n.s
*a*1	r = 0.40 *p* = .0096	n.s	n.s
*a*2	n.s	r = -0.41 *p* = .0082	n.s
λ	n.s	n.s	r = -0.36 *p* = .021
p	n.s	n.s	n.s
w	r = 0.34 *p* = .034	r = -0.38 *p* = .016	N/A
β1	r = 0.64 *p* = 8.55e-06	r = -0.38 *p* = .017	n.s
β2	n.s	n.s	r = 0.42 *p* = .0062
OCD only	MB-I_{Choice}	MB-II_{RT}	*w* - parameter
α-rew	n.s.	r = -0.47 *p* = .035	n.s.
α-neu	n.s.	n.s.	n.s.
*m*1	r = 0.84 *p* = 4.20e-06	r = -0.77 *p* = 5.55e-05	n.s.
*m*2	n.s.	n.s.	r = 0.47 *p* = .035
T1	n.s.	n.s.	n.s.
T2	n.s.	n.s.	n.s.
*a*1	n.s.	n.s.	n.s.
*a*2	n.s.	n.s.	n.s.
λ	n.s.	n.s.	r = -0.63 *p* = .0027

p	n.s.	n.s.	n.s.
w	n.s.	r = -0.63 *p* = .0064	N/A
β1	r = 0.74 *p* = .00017	r = -0.52 *p* = .018	n.s.
β2	n.s.	n.s.	n.s.
CTL Only	MB-I_{Choice}	MB-II_{RT}	*w* - parameter
α-rew	r = 0.57 *p* = .0090	n.s.	n.s.
α-neu	n.s.	n.s.	n.s.
*m*1	r = 0.49 *p* = .030	n.s.	n.s.
*m*2	n.s.	n.s.	n.s.
T1	n.s.	n.s.	n.s.
T2	n.s.	n.s.	n.s.
*a*1	n.s.	n.s.	n.s.
*a*2	n.s.	r = -0.65 *p* = .0020	n.s.
λ	n.s.	n.s.	n.s.
p	n.s.	n.s.	n.s.
w	n.s.	n.s.	NA
β1	r = 0.61 *p* =.0047	n.s.	n.s.
β2	n.s.	n.s.	n.s.
MED- Only	MB-I_{Choice}	MB-II_{RT}	*w* - parameter
α-rew	n.s.	n.s.	n.s.
α-neu	n.s.	n.s.	n.s.
*m*1	n.s.	n.s.	n.s.
*m*2	n.s.	n.s.	n.s.
T1	n.s.	n.s.	n.s.
T2	n.s.	n.s.	n.s.
*a*1	n.s.	n.s.	n.s.
*a*2	n.s.	n.s.	n.s.
λ	n.s.	n.s.	n.s.
p	n.s.	n.s.	n.s.
w	n.s.	r = -0.83 *p* = 0.005962	N/A
β1	r = 0.79 *p* = 0.011	n.s.	n.s.
β2	r = 0.70 *p* = 0.037	n.s.	n.s.
MED+ Only	MB-I_{Choice}	MB-II_{RT}	*w* - parameter
α-rew	n.s.	n.s.	n.s.
α-neu	n.s.	n.s.	n.s.
*m*1	r = 0.96 *p* = 3.70E-06	r = -0.87 *p* = 0.00057	n.s.
*m*2	n.s.	n.s.	n.s.
T1	n.s.	n.s.	n.s.
T2	n.s.	n.s.	n.s.

*a*1	n.s.	n.s.	n.s.
*a*2	n.s.	n.s.	n.s.
λ	n.s.	n.s.	r = -0.66 *p* = 0.026
p	n.s.	n.s.	n.s.
w	n.s.	n.s.	N/A
β1	r = 0.84 *p* = 0.0012	r = -0.72 *p* = 0.013	n.s.
β2	n.s.	n.s.	n.s.

Key: n.s.: non-significant

4.4.5 Summary of Main Results

OCD and CTL were equivalent on all measures of model-based behaviour, namely MB-I_{Choice}, MB-II_{RT}, and *w*. This was also the case when comparing CTL with MED- and MED+. Computational modelling using the standard RL model revealed that OCD had lower β2 values than CTL, indicating OCD showed less exploitation/more exploration during Stage 2. Fitting RL-DDM to data revealed that OCD had reduced *a*2 values compared to CTL, indicating faster and less accurate decisions during Stage 2 in OCD. These group differences were primarily driven by MED+.

4.5 Discussion

This is the first study to formally probe model-based behaviour in adolescents with OCD using a sequential decision-making task originally developed by Daw et al. (2011). To derive reliable and comprehensive estimates of model-basedness, I fit a reinforcement learning-drift diffusion model (RL-DDM) to task data which takes into account choice and response time data (previously done by Shahar et al., 2019). This is an improvement on past studies that have only estimated model-based behaviour based on choices. Modelling choices and reaction times together also enabled greater insight into various latent decision-making processes important for describing behaviour on the task. Contrary to findings from adult OCD studies, adolescents with OCD were equivalent to healthy age-matched controls on all model-based metrics investigated (MB-I_{Choice}, MB-II_{RT}, model-based *w*). Nonetheless, adolescent patients differed from controls in behaviour during Stage 2 of the task, wherein they made more exploratory choices (lower inverse temperature, β2) and favoured speed over accuracy when responding (lower boundary separation parameter, *a*2). These results were primarily driven by patients medicated with SSRIs.

4.5.1 Model-Based Decision-Making

Comparable model-based behaviour between patients and healthy participants across all metrics investigated is firmly indicative of intact age-appropriate model-based reasoning in adolescents with OCD. The finding is unexpected as several studies have reported reduced model-based and goal-directed behaviour in adult OCD patients (Gillan et al., 2014, 2011; Voon, Baek, et al., 2015; Voon, Derbyshire, et al., 2015; Wheaton et al., 2019). This implies that impairments in model-based reasoning only emerge in adulthood in OCD. Perhaps model-based reasoning deteriorates as a function of disorder duration as recent research reports that adult OCD patients with a longer disease duration, compared to patients with shorter disease durations, displayed increased habitual responding on an outcome devaluation task (Chase et al., 2020). As adult patients have lived with the disorder for longer, their cognitive faculties responsible for model-based reasoning may be experiencing greater decline compared to adolescent patients who have acquired the disorder relatively recently.

A slightly different interpretation of these findings could be that OCD disrupts otherwise healthy development of model-based reasoning. This is supported by research showing that young children and adolescents rely primarily on model-free heuristics compared to healthy adults who are more model-based (Decker et al., 2016). Additionally, presence of compulsive symptoms in healthy adolescents has been found to predict slower maturation of model-based behaviour and fronto-striatal regions important for high-order decision-making (Vaghi et al., 2020). Therefore, adolescents with OCD at first show equivalence to healthy adolescents but eventually healthy adolescents go on to strengthen their model-based reasoning while the same behaviour remains stunted in those with OCD, thus accounting for why OCD-related differences in model-basedness are only pronounced in adulthood.

4.5.2 Other features of decision-making

The secondary rationale behind observing behaviour on the current task was to assess general learning and decision-making in adolescents with OCD. The first finding to be discussed here is that adolescents with OCD displayed significantly reduced inverse temperature values corresponding to Stage 2 choices indicating less value-driven responding and more exploration. The exploration parameter did not correlate with boundary separation parameter values (discussed later in this section) in patients, suggesting that quick erratic responding does not necessarily account for increased exploration in this sample. Drift rate scaling parameter values showed a strong association with the tendency to exploit over explore, indicating that participants who were able to discriminate quickly and effectively between various choice values were also more likely to maximise their

rewards. However, drift rate scaling parameter values did not differ significantly between patients and controls, suggesting that choice value sensitivity is more or less intact in patients, but they still have a tendency for exploratory decision-making. Possible explanations for exploration are considered in brief here, but more in-depth discussion is presented in Chapter 7 of this thesis.

Recent computational research employing reinforcement learning tasks and models reveal increased exploration and more switching between choices in adults and children with OCD (Apergis-Schoute et al., in-prep; Hauser et al., 2017; Kanen et al., 2019; Norman et al., 2018). The tasks in these studies contained choice stimuli with probabilistic pay-offs suggesting that stochastic environments are necessary to promote exploratory behaviour in subjects with OCD. Similarly, in the current sequential decision-making task, adolescents with OCD engaged in significantly more exploration during Stage 2, which contains options with outcome probabilities that change frequently throughout the task, but not during Stage 1 which contains options with stable outcome probabilities. Indeed, literature into the explore-exploit dilemma posits that in a dynamic environment, where values of all potential options are uncertain, it is considered conducive for an individual to be able to adapt their behaviour by flexibly alternating between exploratory and exploitative strategies (Addicott, Pearson, Sweitzer, Barack, & Platt, 2017). Empirical research also finds that in healthy people, increasing uncertainty surrounding choice pay-offs promotes more exploratory behaviour (Parr & Friston, 2017; Stojic, Schulz, Analytis, & Speekenbrink, 2020). Patients have been found to experience more subjective uncertainty than healthy people (Stern et al., 2013). Hence, a combination of task uncertainty and subjective uncertainty may be driving abnormal exploration in adolescents with OCD. Patients perhaps feel the need to 'check' alternative options to obtain confirmation that all choices are delivering correct predicted feedback and in the hopes of reducing overall uncertainty. Poor model-based reasoning and/or inaccurate representation of choice values (measured via drift rate scaling parameter) do not seem to account for this over-exploration as metrics corresponding to these measures were equivalent in my patient and control participants.

Alternatively, what appears to be exploration as may be the result of attentional lapses. Poor attention may be impacting learning of values associated with choices or resulting in patients not using learnt value-knowledge to make decisions. In line with this, random, value-less responding is found to be associated with attention-deficit traits in healthy children (Dubois et al., 2020). Attentional deficits are present in adult patients with OCD, as reported by a meta-analysis revealing attentional control in patients to be impaired in across several studies, with moderate effect sizes (Abramovitch et al., 2013). However, evidence is less consistent in child-OCD studies, as so far only two studies have detected attentional impairments in child patients (Baykal et al., 2014; Chang et al.,

2007) while two other studies did not find deficits (Okazaki et al., 2018; Shin et al., 2008). Moreover, another study has only found deficits in attention in child patients with both tic disorder and OCD (Lucke et al., 2014). Thus, it is unclear whether attentional issues are indeed driving this reduced value-driven responding in adolescents with OCD.

There is also evidence for brain regions underlying the use of exploratory strategies (Daw, O'Doherty, Dayan, Seymour, & Dolan, 2006; Domenech, Rheims, & Koechlin, 2020; Laureiro-Martínez, Brusoni, Canessa, & Zollo, 2015; Trudel et al., 2020), namely the ventromedial PFC (vmPFC) and dACC, to be overactivated in patients with OCD (Apergis-Schoute et al., 2018; Fitzgerald et al., 2018, 2010; Huyser et al., 2011; Riesel et al., 2019; Stern et al., 2011, 2013), implying a neural basis for over-exploration in OCD. This is discussed in more detail in the General Discussion (Chapter 7).

The next finding is that adolescents with OCD showed lower boundary separation parameter values than controls on Stage 2 of the task, indicating less evidence accumulation, as well as faster and more error-prone responses. At first, this appears to contradict findings from previous studies modelling decision-making data in OCD using drift-diffusion models, as patients tended to have lower drift rates indicating less choice value sensitivity and more time spent processing evidence (Banca, Vestergaard, et al., 2015; Erhan et al., 2017; Hauser, Moutoussis, et al., 2017; Mandali et al., 2019). However, a closer look at the studies mentioned reveal that the tasks employed were always self-paced, meaning that subjects were under no time pressure to make choices. In fact, Banca et al. (2015) discovered that while adult OCD patients had lower drift rates when the decision-making task being employed was self-paced, introducing a monetary penalty for slowness on some trials led to drastically lower decision boundaries in patients. My findings mirror this as the task I have administered terminates the current trial every time participants fail to answer within an allotted time window. Thus, evidence accumulation in OCD appears to be contingent on task conditions: when given enough time to respond, patients prefer to spend elongated periods accumulating evidence, whereas when penalised for slowness, patients prefer to respond quicker at the expense of accuracy.

It may be that conducting effective evidence accumulation and responding quickly in parallel are too cognitively demanding for patients with OCD, and therefore they default to using one or the other depending on aforementioned task constraints. In the current task, quick error-prone responding may be strategic as responding within the time window confers a chance of receiving a reward whereas spending too long mulling over a decision will lead to the current trial ending with no possibility of a reward. Interestingly, significantly lower decision boundary parameter values were only displayed

by patients in Stage 2 but not Stage 1 of the task. This may be due to outcome probabilities associated with Stage 1 stimuli being stable relative to the slowly changing reward pay-offs associated with the four possible options in Stage 2. Moreover, needing to take into account four different choice values in Stage 2, compared to only two choice values in Stage 1, alongside increased pay-off uncertainty and trial time constraints may have prompted adolescent patients to not attempt to gather evidence and instead turn to quick responding as a strategy. This is perhaps consistent with accounts of altered cognitive control in young people with OCD (Viard et al., 2005), as well as studies showing poor adaptation of response times following feedback (no post-error slowing or post-correct speeding up of responses in patients relative to controls) in adults and children with OCD (Liu, Gehring, Weissman, Taylor, & Fitzgerald, 2012; S. Morein-Zamir et al., 2013).

4.5.3 Medication Effects

Although the OCD group as a whole showed increased exploration and lower boundary separation parameter values during Stage 2, further exploratory analysis revealed that these results were primarily driven by the adolescents with OCD who were receiving SSRI treatment. The reason for this is unclear as, as highlighted in earlier chapters, majority of pertinent research reports superior performance by child and adult patients medicated with SSRIs compared to medication-naïve patients across various cognitive constructs including planning, cognitive flexibility, and feedback learning (Andrés et al., 2008; Lochner, Chamberlain, Kidd, Fineberg, & Stein, 2016; Mataix-Cols, Alonso, Pifarré, Menchón, & Vallejo, 2002; Palminteri, Clair, Mallet, & Pessiglione, 2012). Nonetheless, Apergis-Schoute et al. (in-prep) recently found that adult medicated OCD patients were impaired at contingency learning before reversal on a probabilistic reversal learning task, while pre-reversal learning was intact in unmedicated patients. This suggests that medication may impair instrumental responding and increase shifting behaviour, similar to the exploratory and erratic decision-making displayed by medicated adolescents with OCD in my study.

When conducting correlational analyses, a higher SSRI dosage was found associated with increased IQ, drift rate scaling values, reward rates, and model-based behaviour (measured via MB-II_{RT}). When controlling for IQ, reward rates still showed a significant relationship with SSRI dosage. These findings allude to high dose SSRIs facilitating increased reward sensitivity, and potentially improved IQ scores and model-based reasoning in adolescents with OCD. As mentioned in Chapters 2 and 3, this may be consistent with research reporting that low doses of SSRIs disrupt probabilistic reversal learning in healthy volunteers (Chamberlain, Müller, et al., 2006; Skandali et al., 2018).

As posited in the previous chapter, medicated patients may have had a more severe form of the disorder to have necessitated medication treatment, which could account for their more abnormal decision-making. Nonetheless, this theory cannot account for why previous research has found that SSRIs improve cognitive performance in patients. More research into long-term effects of medication on learning and decision-making in OCD is necessary to derive solid conclusions. Also, as a caveat, there were only 9 unmedicated patients present in my current study and therefore caution must be exercised in interpreting these findings. The medication effects found in the studies presented in this thesis are probed further in the General Discussion chapter (Chapter 7).

4.5.4 Limitations of sequential decision-making task

Despite my successful efforts in deriving holistic metrics of model-based reasoning by accounting for participant choices and response times using RL-DDM, there are still possible limitations to using the sequential decision-making paradigm in its current form to dissociate model-based from model-free strategies. Recently, it has been discovered that people are highly prone to misunderstanding the task's complex instructions leading to inaccurate models of decision-making being captured (Feher da Silva & Hare, 2020). Some common examples of misunderstandings highlighted by Feher da Silva and Hare include 1) subjects believing that one of the Stage 1 choices is 'luckier' than the alternative choice as well as 2) some subjects thinking Stage 2 outcomes after common transitions are more trustworthy or reliable compared to outcomes after rare transitions. These misunderstandings influenced the proportion of first-stage stay responses leading to statistical models labelling subjects as being both model-based and model-free decision makers (Feher da Silva & Hare, 2020). When instructions were improved to eliminate any misunderstandings, subjects actually used predominantly model-based strategies which casts doubt on previous studies reporting that healthy people use a mixture of strategies to solve the task (Daw et al., 2011; Decker et al., 2016; Voon, Derbyshire, et al., 2015). Equally, it is possible that results in my current study were influenced by participants misunderstanding the instructions. Participants with OCD may have been particularly susceptible to this as many patients experience 'magical thinking' or impaired causal reasoning between actions and outcomes (Vaghi et al., 2019). Hence, patients may have imbued their own meaning onto the different transition-types and stimuli used in the task.

Another limitation to this paradigm is that model-free behaviour defined in the task and computational models may not be compatible with actual habit-directed behaviour, despite literature suggesting they are equivalent. Habit-directed behaviour is traditionally defined by the strength of a response cued by a stimulus that is no longer predictive of a rewarding outcome. Hence, habitual behaviour is conducted without the expectation of any outcome and instead actions are triggered

purely by the presence of a stimulus that was associated with rewards in the past. This is distinct from model-free behaviour, which is defined in reinforcement learning models as still being sensitive values associated with choices and their possible outcomes. Recent computational work demonstrates the possibility of conceptualising a truly habit-directed model which is not based on choice values, but is only sensitive to the history of actions taken (Miller et al., 2019). This model may more accurately represent habitual-directed control often reported to be overactive or dominant in OCD (Gillan et al., 2014, 2011; Gillan & Robbins, 2014) compared to the current temporal-difference algorithm used to estimate model-free decision-making.

4.5.5 Conclusions

In this study, I demonstrate that adolescents with OCD can employ model-based control on a sequential decision-making task to a similar extent as healthy adolescents within the same age range. I infer that either impaired model-based reasoning only emerges in adulthood in individuals with OCD or that the disorder disrupts healthy maturation of model-based reasoning over time, which accounts for previous research showing deficits in model-based control in adult OCD patients. However, recent valid criticisms have emerged regarding the administration and modelling of the sequential decision-making task that must be taken into account when interpreting the results. Next, computational modelling of choice and response time data has revealed that adolescents with OCD favour speed over accuracy, and exploration over exploitation when making decisions in Stage 2 of the task. Possible explanations for this include adolescent patients having difficulty arbitrating between different strategies efficiently, deficits in attention and cognitive control, and oversensitivity to stochastic pay-offs (task uncertainty) as well as heightened feelings of subjective uncertainty.

Chapter 5: Meta-Cognition in Adolescent OCD: Are action and confidence dissociated?

5.1 Introduction

Intrusions and compulsions displayed by individuals with OCD are ego-dystonic in nature, as they occur despite being at odds with the core beliefs of the sufferer. Patients continuously engage in maladaptive washing and checking behaviour, for instance, despite having awareness that they are excessive and irrational.

As highlighted in the General Introduction of this thesis (Chapter 1), adults with OCD do not use meta-cognitive information such as confidence to drive their actions. Cognitive research reports that adults with OCD continue to respond to devalued or degraded stimuli despite being aware that the stimuli they are responding to are no longer predictive of outcomes (Apergis-Schoute et al., 2017; Gillan et al., 2014; Vaghi et al., 2019). This dissociation between patients' actions and beliefs has been posited to be due to patients experiencing increased uncertainty surrounding state transitions (how events unfold as a result of specific actions) (Fradkin, Adams, Parr, Roiser, & Huppert, 2020). Patients mistrust or place less weight on prior evidence in their decision-making and hence carry out compulsive behaviours that are at odds with pre-existing information in order to cope with the uncertainty. There is even empirical evidence for this theory, as it was found that adults with high obsessive-compulsive traits assigned lower weights to past feedback information when making decisions on a probabilistic learning task, which led them to regard otherwise expected outcomes as 'surprising' (Fradkin, Ludwig, et al., 2020).

Relevant to the current chapter, Vaghi, Luyckx et al. (2017) used a predictive-inference task to formally test the link between actions and confidence in OCD. Adult patients were tasked with predicting where a coin would land on a screen and rating how confident they were in their predictions being correct. The task was probabilistic in that the coin predominantly landed in the same location with occasional deviations. Bayesian computational modelling revealed that patients updated their confidence levels and predictions separately, confirming the presence of an action-belief dissociation that is prominent in the literature. Confidence levels were correctly updated based on changes in the coin location, but actual predictions did not reflect this knowledge. Instead, patients' predictions were driven by the most recent observation (where the coin landed most recently) instead of accumulated information (where the coin landed most frequently). The disconnect between actions and confidence was even formally probed in a regression model and it

was found that adults with OCD did not update actions and confidence in parallel while healthy adults did. Authors concluded that those with OCD are capable of developing an accurate internal model of the task environment, but fail to use this knowledge to guide their actions. More recently, this confidence-action dissociation has been found to be strongly linked to traits of compulsivity in a large sample of adult subjects (Seow & Gillan, 2020).

Substantially less research has been conducted assessing whether beliefs and actions are also dissociated in youths with OCD. Nonetheless, evidence has emerged from information sampling studies revealing that paediatric patients have higher decision thresholds than typically developing children, which means that patients continue to sample information before making a decision even when sufficient information has already been acquired (Erhan et al., 2017; Hauser, Moutoussis, et al., 2017). This could be suggestive of a dissociation between actions and knowledge, as young patients continue to request information even when doing so no longer has value within the context of the task. Motivation towards acquiring information may instead be internally generated, i.e. to reduce any personal doubt/uncertainty being felt. However, as a caveat, adolescents with OCD were also found to respond similarly to controls during degraded trials on a contingency degradation task and also showed intact action-outcome knowledge (Gottwald, 2017, thesis), suggesting that beliefs and action are relatively interconnected in young patients. Although, this study did not formally assess whether confidence and action were unlinked using a regression model nor did it ascertain whether adolescent patients' actions were being driven by most recent feedback, as was done in Vaghi, Luyckx et al.'s (2017) study in adult patients.

Thus, this study aimed to investigate the relationship between confidence and action in a sample of adolescents with OCD using the predictive-inference task originally employed by Vaghi et al. (2017). In typically developing children, meta-cognition begins to emerge in early adolescence and increases in accuracy with age (Moses-Payne, Habicht, Bowler, Steinbeis, & Hauser, 2020). Thus, it was hypothesised that adolescents with OCD would reveal significantly reduced coupling between confidence and action compared to age-matched healthy adolescents.

5.2 Methods

5.2.1 Sample

Sixty-nine participants in total completed the Predictive-Inference task. Twenty-three participants formed the OCD group while the remaining 46 were in the CTL group. I stopped recruiting control participants for this task after the 46th control to prevent group sizes from being too different between

OCD and CTL groups. Eleven patients from the OCD group were receiving SSRI treatment at the time of the study while 12 were medication-naïve. Eight patients were medicated with sertraline and 4 were medicated with fluoxetine. Mean SSRI dosage was 97.27mg (std dev: 58.33mg) and the dose range was 20 – 200 mg. IQ data was missing from one OCD participant. Further demographic details are outlined in the Results section of this chapter.

5.2.2 Predictive-Inference Task

This paradigm was originally used by Vaghi, Luyckx, et al. (2017), to test for a dissociation between confidence and action in adult patients diagnosed with OCD.

Participants were instructed to try to predict where 'coins' emitting from the center of a circular ring would land by positioning an orange 'bucket' on the same circular ring to catch them (see Figure 5.1). After positioning the bucket, participants had to rate their confidence in their choice on a rating scale ranging from 1 to 100. Before the task began, participants were told that coins mostly flew to approximately the same location, but that location could change sometimes. There was no time limit in each trial, but participants were instructed to respond as quickly and as accurately as possible.

The location the coin would be released to in each trial was mostly determined by sampling a Gaussian distribution. Hence, coins landed in a similar location with small variations driven by noise. The mean of this distribution usually remained stable over a block of trials but changed at random intervals (change-points, see Figure 5.2) when it was resampled from a uniform distribution. The probability of a change-point occurring at any point in a block was set to 0.125. This meant that participants were required to form a new belief about the mean of the Gaussian distribution each time a change-point occurred. There were 360 possible locations for coins to fly to when a change point occurred.

During the task, the bucket could be moved around the ring using a Griffin PowerMate USB rotary controller attached to the testing laptop. Participants confirmed their responses by pressing the spacebar on the laptop keyboard. After 150ms, a confidence bar ranging from 0 to 100 would appear below the ring for participants to indicate how confident they were the coin would land in their bucket. The confidence pointer would always start on a random score between 25 and 75 so participants would be required to change their confidence rating on every trial. After pressing the spacebar again to confirm their confidence rating, a coin was released for 150ms. If the coin landed within the boundaries of the bucket, participants were awarded 10 points, whereas if the coin landed outside the boundaries, they lost 10 points. During correct trials, the bucket would 'flash' by turning white for 1 frame. Additionally, the centre dot would turn green for 800ms and a consonant tone

would be played simultaneously for 400ms. Alternatively, during incorrect trials the centre dot turned red for 800ms and a dissonant tone would play for 400ms (see Figure 5.1)

Stimuli were presented to participants using Matlab R2017b and Psychtoolbox (version 3). Participants completed one practice block of 20 trials and 4 blocks of 75 trials each in the main task. They were allowed to rest in between each block. The duration of the task was 18-20 minutes.

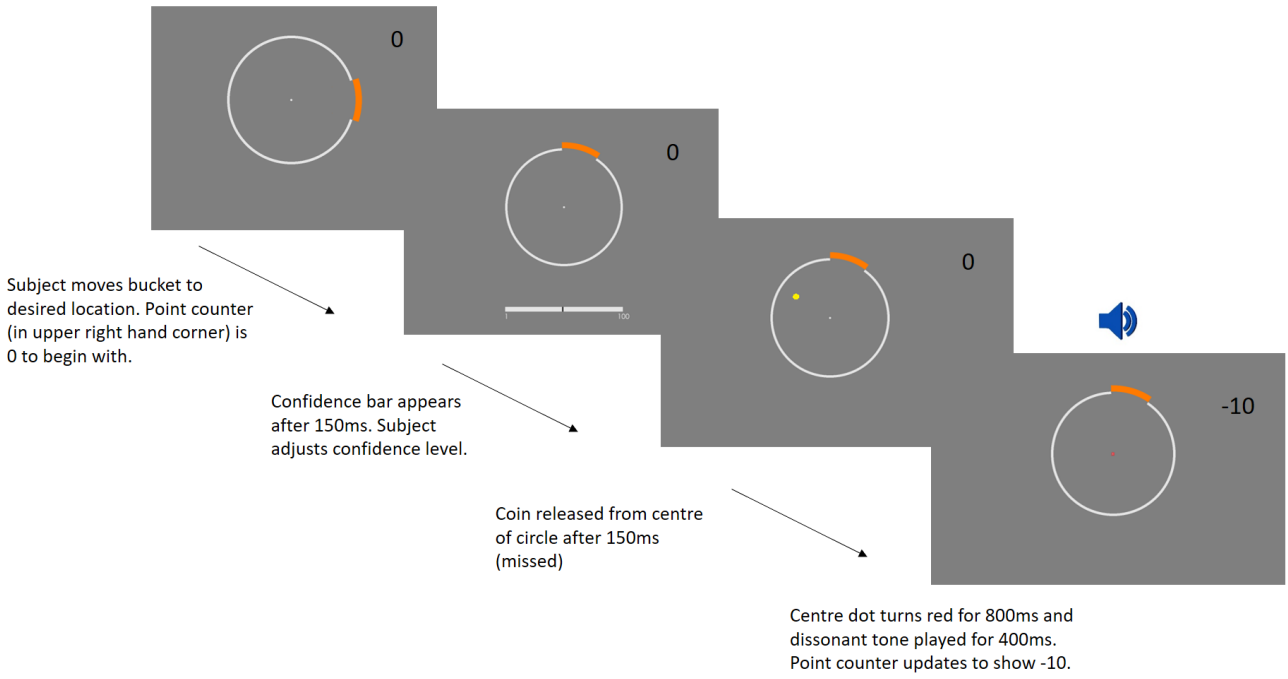

FIGURE 5.9: STIMULUS PRESENTATION OF PREDICTIVE-INFERENCE TASK. THIS IS AN EXAMPLE OF A TRIAL WHERE THE SUBJECT PREDICTED THE COIN LOCATION INCORRECTLY.

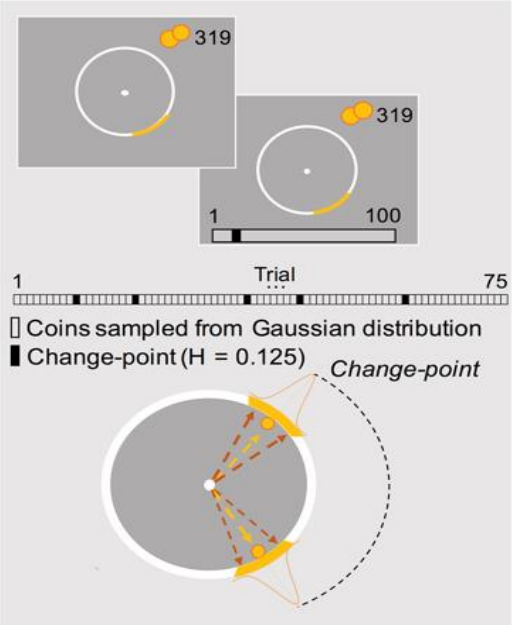

FIGURE 5.10: COIN LOCATIONS ARE DETERMINED USING A GAUSSIAN DISTRIBUTION ON MOST TRIALS. WHEN A CHANGE POINT OCCURS, THE COIN LOCATION CHANGES DRASTICALLY ACCORDING TO A UNIFORM DISTRIBUTION. THE PROBABILITY OF A CHANGE POINT OCCURRING AT ANY POINT DURING THE TASK WAS 0.125. BLACK BARS IN THE FIGURE ABOVE REPRESENT POSSIBLE TRIALS THAT A CHANGE POINT COULD OCCUR IN WITHIN ONE BLOCK. OTHERWISE, COINS ARE SAMPLED FROM A GAUSSIAN DISTRIBUTION (WHITE BARS). FIGURE WAS ADAPTED WITH PERMISSION FROM VAGHI, LUYCKX ET AL. (2017).

5.3 Statistical Analyses

5.3.1 Learning Rate Analysis

Data manipulation and statistical analyses were conducted in Matlab R2017b and RStudio 3.5.0. Analyses and statistical models described here were originally designed and conducted by Vaghi, Luyckx et al. (2017).

For each participant, learning rates on every trial (α_t) were computed to understand how evidence accumulated in the task's noisy environment influenced participants' actions (positioning of the bucket). Learning rates were calculated as follows:

$$\alpha_t = \frac{b_{t+1} - b_t}{\delta_t} \qquad \text{Equation 5.1}$$

$$\delta_t = X_t - b_t \qquad \text{Equation 5.2}$$

In Equation 5.1 and 5.2, b_t and b_{t+1} are the chosen bucket positions at trial t and trial t+1 respectively. δ_t, the spatial prediction error, is the difference between the location of the particle (X_t) at trial t and the position of the bucket at trial t (b_t). Trials where the estimated learning rate (α) exceeded the 95th percentile (calculated separately for each group) or where spatial prediction error was equal to zero were excluded from the analysis. This type of filtering was employed as such extreme values are reported to be due to noisy processes other than error-driven learning (Nassar et al., 2016). It is worth noting that the exclusion threshold used was more stringent than what was employed in Vaghi et al. (2017), who excluded trials exceeding the 99th group percentile. After discussion with Dr. Matilde Vaghi, we decided it was necessary to decrease the cut-off threshold as several trials in our sample revealed extremely high learning rates (α_t>1). A two-sample t-test was used to confirm that there was no significant difference in the proportion of trials removed between the OCD and CTL groups (see 'Data Checks' in Results section). Difference in mean learning rates between groups was then analysed using a Wilcoxon rank-sum test. Additionally, raw confidence ratings were converted to z-scores and a two-sample t-test was used to detect group differences.

To test the effects of spatial prediction error (see Equation 2) on learning rates, the learning rates were divided into 3 quantiles based on magnitude of spatial prediction error (low, medium, and high) using the 'quantile' function in Matlab. For each spatial prediction error quantile, the mean learning rate was computed separately per group (OCD vs CTL). Due to violations of homogeneity of variance and normality, the Welch-James test from the 'welchADF' package in RStudio (Villacorta, 2017) was used to determine the effects of magnitude of spatial prediction error (low, medium, high) and subject group on learning rates. Post-hoc paired Wilcoxon tests with Bonferroni correction were conducted following the main Welch-James test. Magnitude of an effect was determined via a Wilcoxon effect size (Wilcoxon r) calculated by dividing the test z-statistic by the square root of the sample size ($Z/\sqrt{N}$). The following interpretations of effect size values were used, small effect: 0.1 - < 0.3, moderate effect: 0.3 - < 0.5 and large effect: >= 0.5.

5.3.2 Computational Model

Next, to better understand factors influencing trial-by-trial confidence and action updates in participants, a quasi-optimal Bayesian model (previously implemented by Vaghi, Luyckx et al.) was fit to participant data. The model in question is termed a quasi-optimal Bayesian model as it attempts to approximate the behaviour of a full Bayesian learner which would infer future outcomes using information accumulated over all previous outcomes (Nassar et al., 2010), but using the less computationally complex delta rule. The delta rule (see Equation 5.3) involves updating a future belief (at t+1) based on the current belief and the error made in predicting the most recent outcome

(δ_t). The influence of the new outcome over beliefs (B_t) is controlled by a learning rate (α_t). At $\alpha_t = 0$, the model's belief is not changed following incoming outcome information at all, while at $\alpha_t = 1$ the most recent outcome will completely influence the model's beliefs.

$$B_{t+1} = B_t + \alpha_t \text{ x } \delta_t \qquad \text{Equation 5.3}$$

The prediction error, δ_t is defined as the difference between the current belief about the coin's location, B_t, and the actual location of the coin, X_t:

$$\delta_t = X_t - B_t \qquad \text{Equation 5.4}$$

In turn, the model's learning rate, α_t, is defined as:

$$\alpha_t = \Omega_t + (1 - \Omega_t)(1 - \nu_t) \qquad \text{Equation 5.5}$$

α, in the above equation, was dynamic meaning it could change from trial-to-trial (as opposed to α parameters in other reinforcement learning studies which are kept constant). Ω_t in Equation 5.5 represents the change-point probability, indicating how likely the model thinks a change in location has occurred. α_t increases when the model assumes a change-point is likely to have taken place. This change point probability, Ω_t, is constructed as the relative likelihood that a new location will be drawn from the same Gaussian distribution (N) centred around the current belief, B_t of the model, or alternatively from a uniform distribution over 360 possible locations:

$$\Omega_t = \frac{(X_t|1,360)H}{(X_t|1,360)H + N(X_t|B_t, \sigma^2{}_t)(1-H)} \qquad \text{Equation 5.6}$$

H in the equation above represents the hazard rate (the actual probability that the mean distribution has changed at any given trial). H was fixed at 0.125. Ω_t will be close to 1 when the probability of the sample coming from a uniform distribution is higher than the probability of it being drawn from a Gaussian distribution (indicating a surprising outcome).

$\sigma^2{}_t$ in Equation 5.6 is the estimated variance of the predictive distribution and is influenced by the variance of the generative Gaussian distribution $\sigma^2{}_N$ (noise in the location of the sample before a change point has occurred) and model confidence, ν_t:

$$\sigma^2{}_t = \sigma^2{}_N + \frac{(1-\nu_t)\sigma^2{}_N}{\nu_t} \qquad \text{Equation 5.7}$$

Lastly, model confidence, *v*, in Equation 5.5 is always computed for the subsequent trial, and takes into account uncertainty arising from imprecise estimation of the mean of the sample location:

$$v_{t+1} = \frac{\Omega_t\sigma^2{}_N+(1-\Omega_t)(1-v_t)\sigma^2{}_t+\Omega_t(1-\Omega_t)(\sigma^2{}_t\, v_t)^2}{\Omega_t\sigma^2{}_N+(1-\Omega_t)(1-v_t)\sigma^2{}_t+\Omega_t(1-\Omega_t)(\sigma^2{}_t\, v_t)^2+\sigma^2{}_N} \qquad \text{Equation 5.8}$$

There are 3 terms included in the numerator (from left to right): 1) reflects the variance when a change point is thought to have occurred, 2) represents variance when no change point is assumed to have occurred, and finally 3) reflects a rise in uncertainty when the model is unsure about whether a change point has occurred or not. The 3 terms from the numerator are repeated in the denominator with an added variance term reflecting uncertainty arising from noise in the Gaussian distribution. When an unexpected change in the task environment occurs, model confidence will decrease, and as a result, the learning rate, α_t in Equation 5.5 will increase.

5.3.3 Influence of Model Parameters on Learning and Confidence

Linear regressions were run to estimate how much participants updated their actions and confidence over time according to parameters from the Bayesian model. Each regression model contained parameters from the model as predictors, namely absolute prediction error, change point probability, and the inverse of model confidence (relative uncertainty), which reflects uncertainty arising from inaccurate estimation of the mean coin position. Relative uncertainty was inserted as (1- Ω)*(1-v) in the regression models which is consistent with the term in Equation 5.5. Hit/miss was also inserted as a categorical variable to assess whether human action and confidence was influenced by immediate positive feedback.

For the action regression model, the dependent variable, 'action' was constructed similar to the belief update formula of the Bayesian model (Equation 5.3), by multiplying the learning rate, α_t, by the absolute prediction error, $|\delta_t|$. If participant behaviour mimicked that of the Bayesian model, action would be suitably influenced by spatial prediction error, change point probability, and model confidence, but not by hit/miss feedback. Within the confidence regression model, z-scored reported confidence was included as the dependent variable. Since confidence rises as uncertainty decreases, negative regression slopes/beta coefficients were expected for the change-point probability and relative uncertainty parameters. The last trial of each block per participant was removed before conducting the regressions as learning rates could not be estimated from these trials. Goodness-of-fit of each model to participant data was assessed by extracting median R-squared values, which was also done in Vaghi, Luyckx et al. (2017).

To formally examine whether confidence and action are uncoupled in adolescent patients, a third linear regression model was conducted with absolute confidence update (absolute difference between z-scored confidence scores on trial t and t-1) as the independent variable and absolute action update (absolute difference between where bucket was positioned at trial t and t-1) as the dependent variable. If confidence and action were linked, increased adjusting of bucket position (action) would correspond to a similar magnitude of changes in confidence ratings.

To ascertain the presence of group differences in performance, beta coefficients associated with each predictor across the three regressions were extracted and compared between patients and controls. Independent sample t-tests were employed for these comparison analyses. Wherever the homogeneity of variance assumption was violated the Welch's independent t-test was used instead. Additionally, if the normality assumption was violated the Wilcoxon rank sum test was used. Cohen's *d* was calculated as a measure of effect size whenever a significant effect of group was detected. The following interpretations of effect size values were used, small effect: <= 0.2 - <0.5, moderate effect: 0.5 > - < 0.8 and large effect: >= 0.8.

Correlations between task measures (learning rates, confidence scores, and regression beta values) and clinical and intelligence scores were quantified using Pearson's correlation coefficient (Pearson's r).

Finally, the analyses described above were re-run but this time comparing behaviour on the task between 3 independent groups, CTL, MED-, and MED+. These exploratory analyses were conducted to examine whether the proposed action-confidence dissociation displayed by patients with OCD was modulated by SSRIs. I first checked whether there was a difference in learning rates between the three groups using the data that was filtered using a 95% threshold for CTL and OCD separately. The analyses were then repeated using data that was filtered using a 95% threshold for CTL, MED-, and MED+ groups.

5.4 Results

5.4.1 Analyses by Group (CTL vs OCD)

Sixty-nine participants in total completed the Predictive-Inference task. Twenty-three participants formed the OCD group while the remaining 46 were in the CTL (healthy control) group. Table 5.1 summarises the demographic and clinical characteristics for both groups. Groups were matched for gender, age, and IQ (intelligence quotient) scores. However, OCD had significantly elevated depression, anxiety, and obsessive-compulsive severity scores compared to CTL.

Table 5.1: Mean scores and standard deviations per group and measure.

	CTL (n = 46)	**OCD (n = 23)**	**STATISTIC**
GENDER(F:M)	28/18	14/9	$\chi 2$ (1)=0, p = 1
AGE	16.59 ± 1.78	15.95 ± 1.67	t(67) = 1.44; p = .15
WASI-II (IQ)[a]	107.61 ± 11.62	108.32 ± 13.80	t(66) = -0.22; p = .83
BDI **	46.46 ± 5.27	58.35 ± 8.95	t(29.84) = -5.88; p = 2.96e-06
BAI **	45.98 ± 7.66	66.30 ± 9.55	Z = -6.52; p = 6.85e-11
OCI **	8.13 ± 6.49	30.74 ± 14.08	Z = -5.93; p = 2.99e-09
CY-BOCS	N/A	23.45 ± 5.19	N/A

Key: CTL: Control Group; OCD: Obsessive-Compulsive Disorder group; WASI-II: Wecshler's Abbreviated Scale of Intelligence – II; IQ: Intelligence Quotient; BDI: Beck's Depression Inventory (t-scored); BAI: Beck's Anxiety Inventory (t-scored); OCI: Obsessive-Compulsive Inventory; CY-BOCS: Child Yale-Brown Obsessive-Compulsive Scale. *p<.05; **p<.01; [a] missing data from one OCD participant.

Learning Rate and Spatial Prediction Error

There was a trend for OCD (0.87 ± 0.56) to show increased learning rates compared to CTL (0.61±0.25), Z = -1.92; p = .055 (see Figure 5.3).

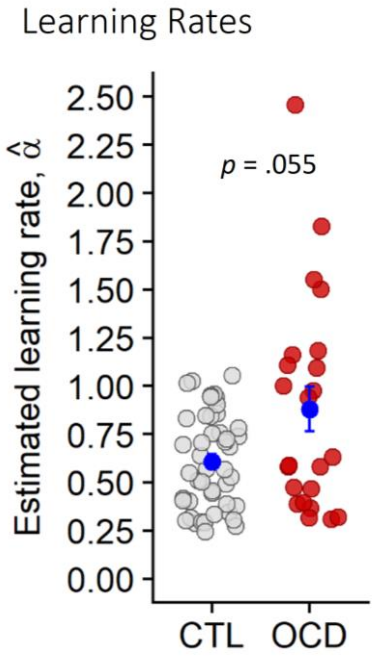

FIGURE 5.11: MEAN LEARNING RATES FOR CTL AND OCD. GROUPS DID NOT DIFFER SIGNIFICANTLY FROM EACH OTHER (P = .055).

Z-scored confidence ratings did not differ significantly between groups, $t(67) = 1.30$; $p = .20$.

Next, after dividing the learning rates by magnitude of spatial prediction error (Low, Medium, High), I found a significant main effect of Error Magnitude $T_{wj}(2,28.80) = 66.76$, $p = 1.54e\text{-}11$; $\eta 2 = 0.037$, wherein learning rates were higher at High (0.81±0.80) magnitudes compared to Medium (0.56±0.34) magnitudes, (Wilcoxon test: Z =-5.53; $p = 3.15e\text{-}08$; Wilcoxon's r = 0.46). There were no significant differences in learning rates between Low (0.82±1.11) and Medium ($p = .597$) and Low and High magnitudes ($p = .058$).

Importantly, a significant Group-by-Error Magnitude interaction was detected (see Figure 5.4), $T_{wj}(2,28.80) = 4.37$, $p = .022$; $\eta 2 = 0.076$. Post-hoc Wilcoxon tests revealed that OCD (1.41±1.68) displayed higher learning rates compared to CTL (0.53±0.46) in response to Low error magnitudes (Z =-2.52; $p = .012$; Wilcoxon's r =0.30). There were no group differences in learning rates at Medium (CTL: 0.53±0.30; OCD: 0.63±0.41; $p = .49$) and High (CTL: 0.80±0.11; OCD: 0.82±0.13; $p = .95$) error magnitudes.

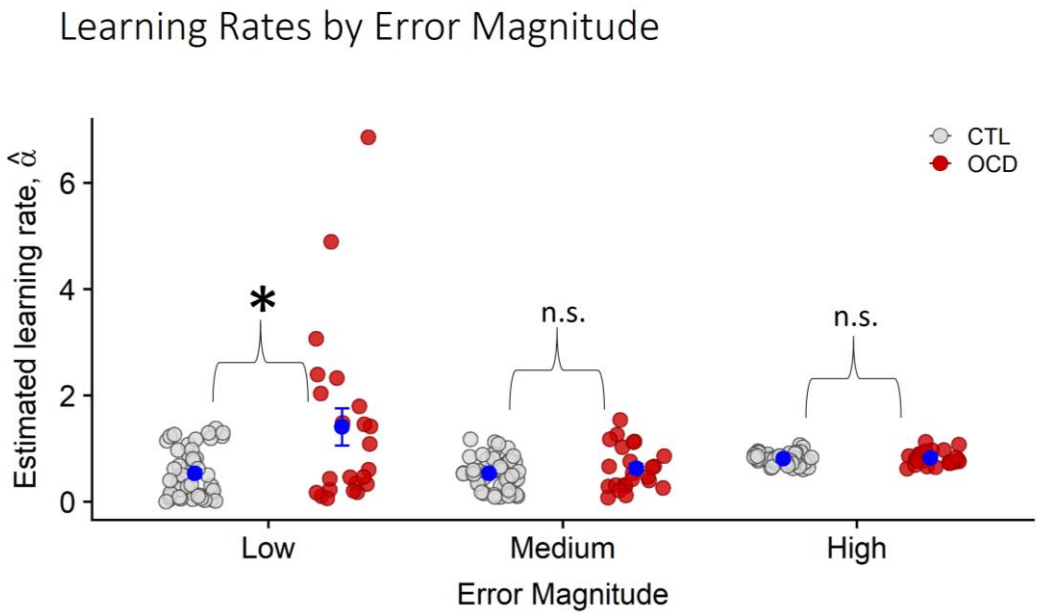

FIGURE 5.12: MEAN LEARNING RATE PER GROUP BINNED ACCORDING TO ERROR MAGNITUDE (SPATIAL PREDICTION ERROR). OCD SHOWED INCREASED LEARNING RATES COMPARED TO CTL AT LOW ERROR MAGNITUDES.

Regression Models

The median r-squared values for the action regression model were CTL: 0.87 and OCD: 0.80, while the median r-squared values for the confidence regression model were CTL: 0.09 and OCD: 0.06.

These estimates of goodness-of-model fit were similar to the median r-squared values reported in Vaghi et al.'s study (action: CTL – 0.81, OCD – 0.85; confidence: CTL – 0.15, OCD – 0.11).

The action and confidence regression results are summarised in Table 5.2 and 5.3 respectively as well as in Figure 5.5. In the confidence model, confidence scores were more influenced by prediction errors in CTL (Beta Coefficients: -0.086±0.13) compared to OCD (Beta Coefficients: -0.0067±0.15), t(67) = -2.26; p = .027; Cohen's d = 0.58. There were no other group differences in parameter values in the confidence model. Additionally, there were no group differences in any of the beta values corresponding to parameters in the action model.

Table 5.2: Summary of parameters for CTL and OCD obtained from Action regression model

Parameter	Group	Mean Beta	Standard Dev.	Analyses used	Statistics
PE	CTL	0.43	0.30	Two-sample t-test	t(67) = 0.50; p =.62
	OCD	0.39	0.32		
CPP	CTL	0.47	0.29	Two-sample t-test	t(67) = 0.017; p =.99
	OCD	0.46	0.28		
RU	CTL	0.71	0.67	Two-sample t-test	t(29.86) = -1.2, p = .24
	OCD	1.02	1.13		
Hit/Missed	CTL	-0.74	0.24	Welch Two-sample t-test	t(67) = 0.40; p = .69
	OCD	-0.76	0.32		

Key- PE: prediction error, CPP: Change Point Probability, RU: Relative Uncertainty

Table 5.3: Summary of parameters for CTL and OCD obtained from Confidence regression model

Parameter	Group	Mean Beta	Standard Dev.	Analyses used	Statistics
PE	CTL	-0.086	0.13	Two-sample t-test	t(67) = -2.26; p = .027; Cohen's d = 0.58
	OCD	-0.0067	0.14		
CPP	CTL	-0.118	0.21	Two-sample t-test	t(67) = 1.19; p = .24
	OCD	-0.186	0.25		
RU	CTL	-0.168	0.15	Two-sample t-test	t(67) = -0.40; p = .69
	OCD	-0.151	0.18		
Hit/Missed	CTL	0.156	0.12	Two-sample t-test	t(67) = 1.61; p = .11
	OCD	0.104	0.13		

Key- PE: prediction error, CPP: Change Point Probability, RU: Relative Uncertainty

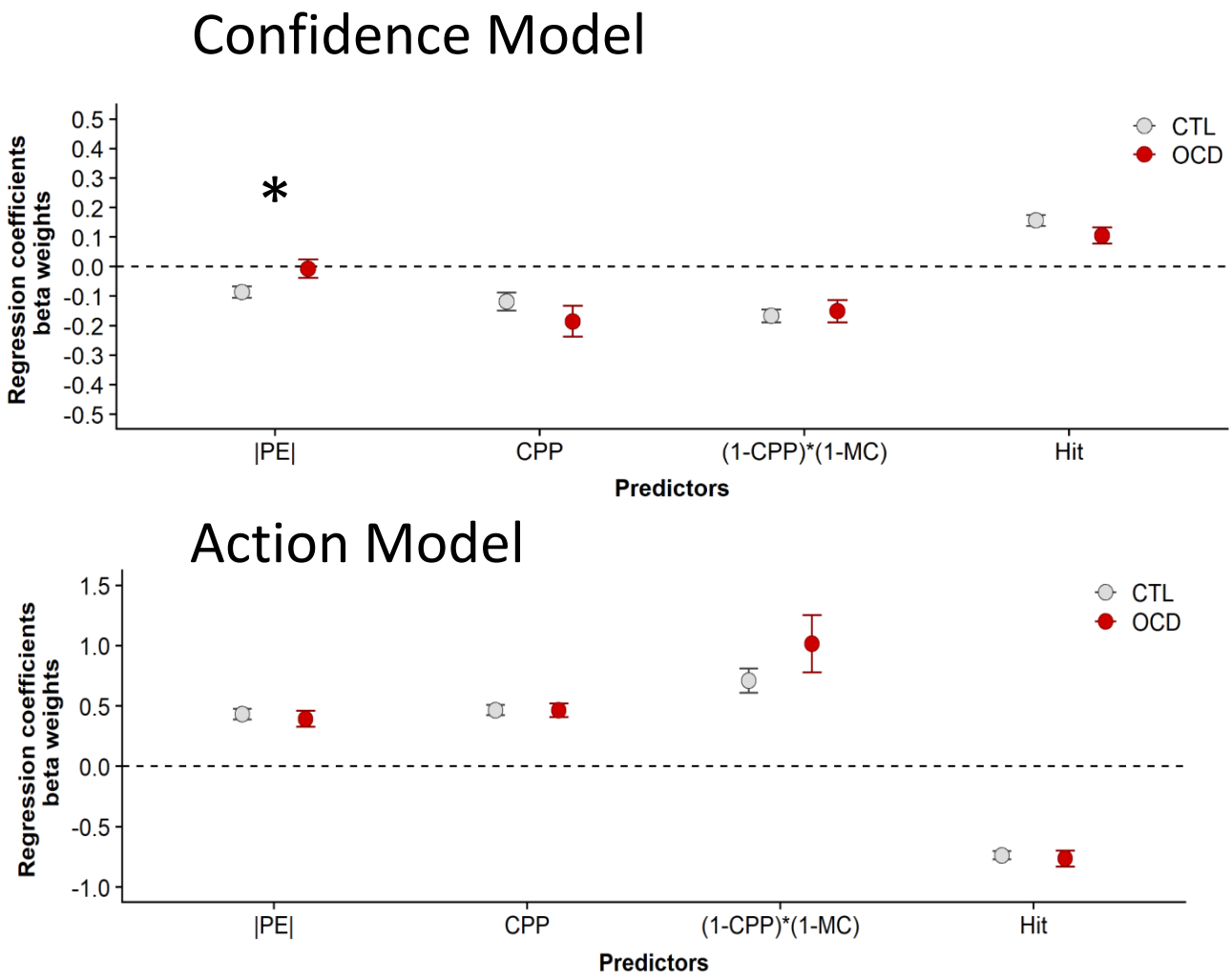

FIGURE 13.5: REGRESSION MODELS FOR CONFIDENCE (TOP) AND ACTION (BOTTOM). |PE|: ABSOLUTE PREDICTION ERROR; CPP: CHANGE POINT PROBABILITY; (1-CPP)*(1-MC): RELATIVE UNCERTAINTY; HIT: HIT/MISSED FEEDBACK. CTL SHOWED LOWER CONFIDENCE SCORES FOLLOWING PREDICTION ERRORS COMPARED TO OCD.

Next, the confidence-action regression model revealed no group differences in degree of action-confidence coupling (CTL: 0.053 ± 0.064; OCD: 0.050 ± 0.084; $t(34.99) = 0.11$, $p = .91$) (see Figure 5.6).

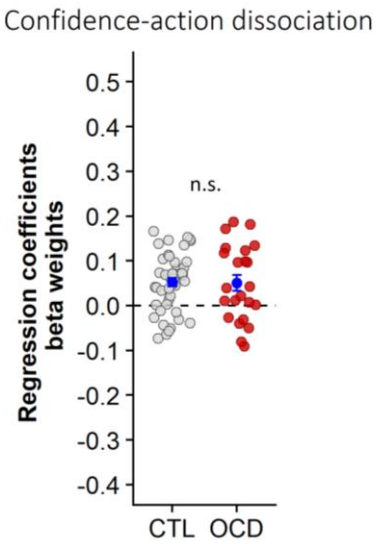

FIGURE 5.14: CONFIDENCE-ACTION DISSOCIATION REGRESSION BETAS. NO GROUP DIFFERENCES WERE DETECTED IN ACTION-CONFIDENCE COUPLING.

5.4.2 Medication Exploratory Analyses

In this section, OCD were further grouped into MED+ (medicated) and MED- (unmedicated). The groups still displayed no significant differences in gender, age, and IQ (see Table 5.4).

Table 5.4: Mean scores and standard deviations per group and statistical test.

	CTL (n = 46)	**MED- (n = 12)**	**MED+ (n = 11)**	**STATISTIC**	**PAIRWISE COMPARISONS**
GENDER(F:M)	28/18	8/4	6/5	$\chi2$ (2)=0.35 , p = 0.84	-
AGE	16.59 ± 1.78	15.87 ± 1.60	16.04 ± 1.81	$\chi2$ (2)=4.50 , p = 0.11	-
WASI-II (IQ)[a]	107.61 ± 11.62	109.82 ± 12.99	106.82 ±15.03	F(2,65) = 0.19, p=0.83	-
BDI **	46.46 ± 5.27	56.67 ± 9.52	60.18 ± 8.33	F(2,66) = 42.1, p=1.64e-12	CTL < MED- & MED+ MED- = MED+
BAI **	45.98 ± 7.66	66.08 ± 9.53	66.55 ± 10.03	$\chi2$ (2)=42.57 , p = 5.7e-10	CTL < MED- & MED+ MED- = MED+
OCI **	8.13 ± 6.49	32.33 ± 14.74	29.00 ± 13.82	$\chi2$ (2)=35.30 , p = 2.159e-08	CTL < MED- & MED+ MED- = MED+
CY-BOCS	N/A	24.73 ± 5.88	22.18 ± 4.29	t(20) = 1.16; p=0.26	N/A

Key: CTL: Control Group; MED-: Unmedicated patient group; MED+: Medicated patient group; WISC-IV: Wechsler's Abbreviated Scale of Intelligence – II; IQ: Intelligence Quotient; BDI: Beck's Depression Inventory (t-scored); BAI: Beck's Anxiety Inventory (t-scored); OCI: Obsessive-Compulsive Inventory; CY-BOCS: Child Yale-Brown Obsessive-Compulsive Scale. *p<.05; **p<.01; [a] missing data from one MED- participant.

Post-hoc tests revealed that compared to CTL, MED+ and MED- groups had elevated depression (Pairwise t-tests, MED- vs CTL: t(66) = 4.72; p = .000038, MED+ vs CTL: t(66) = 6.13; p = 1.66e-06), anxiety (Dunn's test, MED- vs CTL: p = 5.60e-07, MED+ vs CTL: p = 2.25e-06), and obsessive-compulsive scores (Dunn's tests, MED- vs CTL: p = 3.18e-06, MED+ vs CTL: p = 5.23e-05). There were no differences on these measures between MED- and MED+ (all p > .05).

First, I divided the learning rates (filtered by OCD and CTL) into CTL, MED-, and MED+ groups. A Kruskal-Wallis test revealed a significant effect of group on the learning rates, $\chi2$ (2) = 8.03, p = .034, $\eta2$ = 0.072. Post-hoc Wilcoxon pairwise tests indicated that MED- (0.97±0.47) had significantly increased learning rates compared to CTL (0.61±0.25), Z = -2.37, p=.018, Wilcoxon r

= 0.36. Conversely, CTL and MED+ (0.78±0.66; p=1.00), as well as MED- and MED+ (p=.57) showed comparable learning rates to one another.

Following this result, I then decided to filter out trials with learning rates that were greater than the 95th percentile for each of the 3 groups, identical to what was done for the OCD vs CTL analysis. A Kruskal-Wallis test on these newly filtered learning rates still showed a significant group effect, $\chi 2$ (2) = 9.16, p = .010; $\eta 2$ = 011. Post-hoc Wilcoxon tests continued to reveal a difference in learning rates between MED- (1.07±0.49) and CTL (0.61±0.25), Z= -2.97; p=.03; Wilcoxon's r = 0.41 (see Figure 5.7). Other pairwise comparisons were not significant (MED+ = MED-, p=.35; MED+ = CTL, p=1.00). Additionally, z-scored confidence ratings were comparable across the 3 groups (F(2,66) = .901; p = .41).

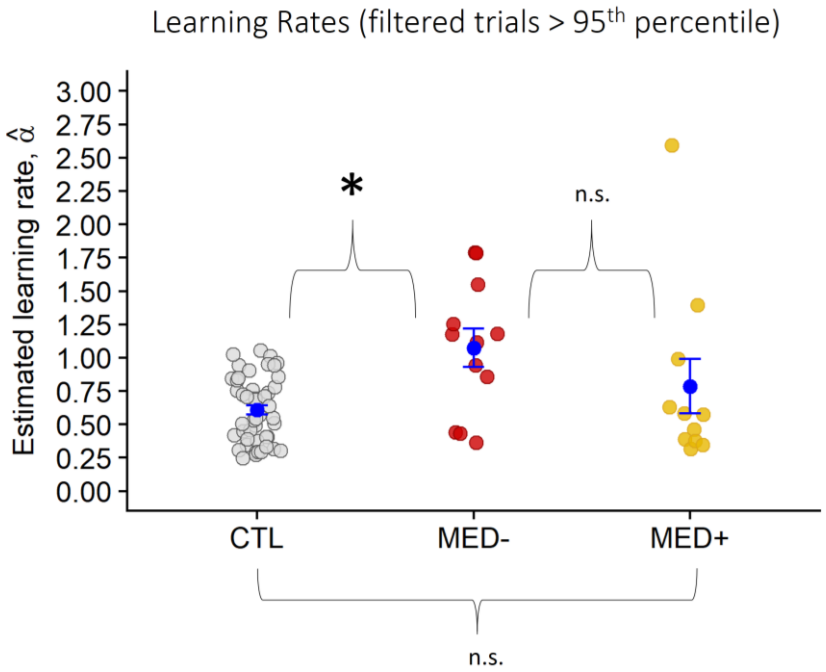

FIGURE 5.15: LEARNING RATES BY GROUP. LEARNING RATES FOR MED- WERE SIGNIFICANTLY HIGHER THAN CTL. MED+ = CTL AND MED- = MED+.

Next, after dividing learning rates by spatial prediction error magnitudes, there was a significant effect of Group (T_{wj}(2,14.92) = 4.68, p = .026), Error Magnitude (T_{wj}(2,19.56)=58.96, p = 5.22e-09), and Group x Error Magnitude (T_{wj}(4,17.14)=4.00 , p = .018) (see Figure 5.8). Post-hoc Wilcoxon tests indicated that MED- (1.93±1.41) had higher learning rates at Low error magnitudes compared to CTL (0.53±0.46), Z = -4.18, p = 2.98e-5, Wilcoxon's r = 0.51. Learning rates at low error magnitudes were equivalent between MED+ (1.25±2.21) and CTL (p = 1.00), as well as between MED- and MED+ (p = .15).

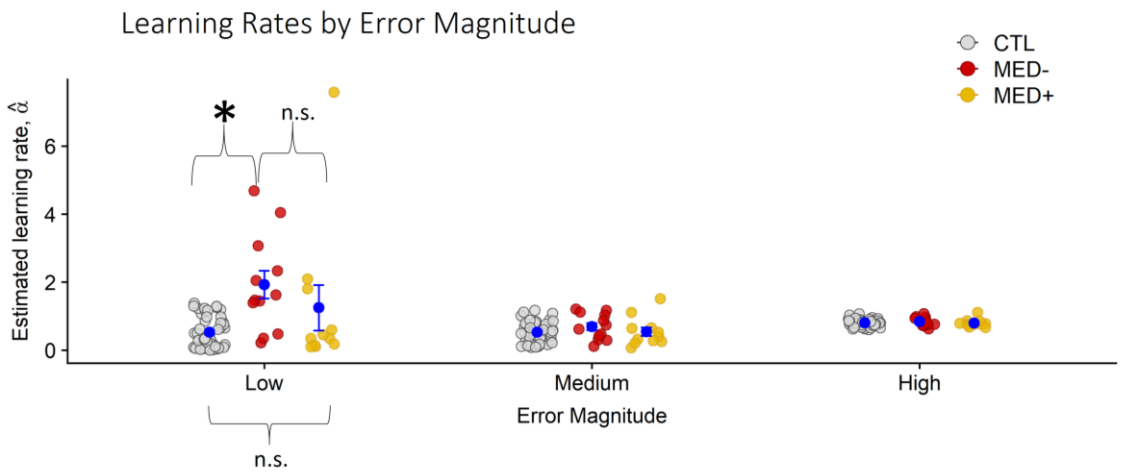

FIGURE 5.16: LEARNING RATES DIVIDED INTO LOW, MEDIUM, AND HIGH ERROR MAGNITUDES. MED- SHOWED SIGNIFICANTLY INCREASED LEARNING RATES COMPARED TO CTL DURING LOW ERROR MAGNITUDES.

Next, the median r-squared values for the regression models were as follows: action regression, CTL = 0.87, MED+ = 0.76, MED- = 0.81; confidence regression, CTL =0.085, MED+ = 0.073, MED- = 0.048.

There were no significant group differences in beta values across all parameters included in the action and confidence regression models (see Table 5.5 and 5.6).

Table 5.5: Summary of parameters for CTL MED- and MED+ obtained from Action regression model

Parameter	Group	Mean Beta	Standard Dev.	Analyses used	Statistics
PE	CTL	0.43	0.30	One-Way ANOVA	$F(2,66) = 0.052$, $p = .95$
	MED-	0.43	0.37		
	MED+	0.40	0.31		
CPP	CTL	0.47	0.29	One-Way ANOVA	$F(2,66) = 1.11$, $p = .33$
	MED-	0.41	0.31		
	MED+	0.48	0.26		
RU	CTL	0.71	0.67	One-Way ANOVA	$F(2,66) = 0.53$; $p = .59$
	MED-	0.93	1.33		
	MED+	1.01	0.94		
Hit/Missed	CTL	-0.74	0.24	One-Way ANOVA	$F(2,66) = 0.69$; $p = .51$
	MED-	-0.85	0.28		
	MED+	-0.70	0.35		

Key- PE: prediction error, CPP: Change Point Probability, RU: Relative Uncertainty

Table 5.6: Summary of parameters for CTL, MED-, and MED+ obtained from Confidence regression model

Parameter	Group	Mean Beta	Standard Dev.	Analyses used	Statistics
PE	CTL	-0.086	0.13	One-Way ANOVA	$F(2,66) = 2.38$, $p = .10$
	MED-	0.013	0.16		
	MED+	-0.037	0.18		
CPP	CTL	-0.12	0.21	One-Way ANOVA	$F(2,66) = 1.48$, $p = .24$
	MED-	-0.15	0.26		
	MED+	-0.21	0.28		
RU	CTL	-0.17	0.15	One-Way ANOVA	$F(2,66) = 0.53$; $p = .59$
	MED-	-0.12	0.17		
	MED+	-0.18	0.20		
Hit/Missed	CTL	0.16	0.12	One-Way ANOVA	$F(2,66) = 0.69$; $p = .51$
	MED-	0.088	0.13		
	MED+	0.13	0.12		

Key- PE: prediction error, CPP: Change Point Probability, RU: Relative Uncertainty

Lastly, there were no group differences in beta values for the action-confidence coupling regression (CTL: 0.054 ± 0.065, MED-: 0.043 ± 0.090, MED+: 0.071 ± 0.076; $F(2,66) = 0.442$, $p = 0.645$), indicating that action and confidence were coupled to the same extent in all groups.

5.4.3 Correlation Analysis

Across all participants, lower IQ was associated with increased learning rates ($r = 0.28$, $p = .020$). However, this significant correlation was no longer present when doing separate group analyses (CTL: $p = .13$; OCD: $p=.87$).

Within MED+, elevated depression scores were associated with lower learning rates ($r = -0.74$, $p = .0087$). Medication dosage correlated with IQ scores ($r =0.61$, $p = .049$).

Next, within MED-, IQ showed a negative relationship with confidence scores ($r =-0.68$, $p = .021$), but the opposite relationship emerged in MED+ ($r = 0.77$, $p = .0055$).

No other significant relationships between task measures and clinical/demographic/intelligence measures were detected.

5.4.4 Overall Data Checks

After filtering trials that exceeded the 95th percentile per group, I checked that there were no statistical differences in proportion of trials removed for the OCD and CTL groups, (mean proportion removed: CTL = 0.065±0.044; OCD = 0.064±0.052; $F(1,67) = 0.0044$, $p = .95$), as well as for CTL, MED-, and MED+ groups (mean proportion removed: CTL: 0.087±0.045, MED-: 0.066±0.081, MED+: 0.045±0.029; $F(2,66) =1.97$, $p = .15$).

Next, it was verified that CTL and OCD showed overall comparable performance on the task as there was no significant difference in mean number of points gained between groups, $t(67) = 0.62$, $p= .54$. There were also no performance differences between CTL, MED+, and MED- ($F(2,66) = 0.96$; $p= .40$).

5.4.5 Summary of Main Results

When dividing participants by OCD and CTL, OCD revealed a trend for increased learning rates overall. These elevated learning rates were most apparent in OCD when spatial prediction error magnitudes (difference between belief about location and actual location) were low. When analysing groups by medication status, increased learning rates at low error magnitudes were driven primarily by MED-. The regression analyses revealed no striking differences between groups aside from CTL making lower confidence ratings according to magnitude of spatial prediction errors compared to OCD, although this pattern ceased to be significant when dividing participants by medication status.

All participant groups showed similar levels of coupling between action and confidence as demonstrated in the action-confidence regression analyses.

5.5 Discussion

This study sought to investigate the relationship between action and confidence in adolescents with OCD compared to typically developing adolescents. The paradigm used was previously implemented by Vaghi, Luyckx et al., (2017) who uncovered a novel dissociation between action and confidence in adults with OCD, in addition to increased action updating following recent feedback in this clinical population. Distinct from their adult counterparts, adolescents with OCD showed similar levels of action-confidence coupling to matched controls. Furthermore, overactive action updating in OCD was only prominent during low spatial prediction errors, which is in contrast to adult patients who had displayed abnormally enhanced updating at every magnitude of prediction error (Vaghi, Luyckx, et al., 2017). Increased learning rates following low prediction errors was driven primarily by the unmedicated patients. Lastly, the adolescent OCD group's confidence ratings were less influenced by prediction errors compared to healthy controls.

5.5.1 Increased learning rates in OCD

Heightened learning rates displayed by adult patients in Vaghi, Luyckx et al.'s study was posited to indicate patients' choices were influenced largely by most recent outcomes rather than information accumulated over time. In contrast, healthy adults understood that the best strategy, before a change point occurred, was to position the bucket in the position with the highest likelihood for a coin to land. This finding is emphasised in that study's regression analysis whereby adult patients' actions were most affected by prediction errors and not change point probabilities.

By contrast, adolescents with OCD only updated actions excessively following low prediction errors, suggesting they are not as sensitive to recent negative feedback as adults with the disorder. In fact, the lack of group differences within the action regression model is likely attributed to patients updating their actions similarly to controls following other magnitudes of prediction error. Excessive updating at low prediction errors demonstrate that patients are 'tracking' the location of the coin by moving the bucket every time the coin makes a small deviation from its last location. One line of reasoning for this behaviour is that the OCD group are pre-occupied with ensuring the coin lands with high certainty in the middle of the bucket. As an anecdote, when I asked two participants with OCD about their experiences with the task, they reported that they were simply following the location of the coin to make sure that it landed into the bucket. This is very evocative of not-just-right

perception (where a sufferer has internal feelings of incompleteness or that their environment is not as it should be) often present in OCD. In actual fact, 59% of paediatric OCD patients describe having not-just-right related obsessions (Nissen & Parner, 2018), and they are even present in biological parents of OCD patients (Sica, Bottesi, Caudek, Orsucci, & Ghisi, 2016). Trials where the coin just barely lands in the bucket may have triggered a not-just-right perception in the OCD group, leading to the urge to re-arrange the bucket. Indeed, ordering/symmetry-related compulsions, like what is seen here, are strongly associated with not-just-right perceptions (Coles, Frost, Heimberg, & Rhéaume, 2003).

These frequent, albeit small, choice corrections done by adolescents with OCD, are consistent with numerous studies reporting increased error-related negativity (ERN) in paediatric OCD patients (see Chapter 1). Importantly, these error signals are generated in the absence of feedback and are instead triggered by a person's own awareness that an error has indeed occurred (Potts et al., 2012). Heightened ERN in OCD could be likened to an internal 'alarm bell' that frequently sounds despite low volatility in the external environment. In line with this, Fradkin, Adams et al.'s (2020) computational model of OCD proposes that feeling excessively uncertain about the objectively stable environment leads to patients perceiving that their rituals are not performed adequately culminating in a tendency to repeat actions. Hence, uncertainty about the environment exacerbated by (or contributing to) abnormal ERN signals could be driving excessive action updating/correcting in the current task, even when there is nothing to correct.

Moreover, frequent choice updating in this task could be a form of increased information gathering, which has been observed prior in youths with OCD on information sampling (Hauser, Moutoussis, et al., 2017) and perceptual decision-making tasks (Erhan et al., 2017). In these studies, young patients accumulated more information than controls even when they had collected more than enough information to form a correct response. Patients in my study could be executing a similar type of behaviour where they are adjusting their choices to gather more information about the most optimal location. Increased perceptual uncertainty, as discussed earlier, could be driving this need to gather more information. Alternatively, patients may be taking a longer time than controls to learn the exact optimal location to place the bucket, which would be compatible with research suggesting that youths with OCD have a learning deficit (Gottwald et al., 2018; Vloet et al., 2010). Nonetheless, behaviour on this current task in OCD is only divergent from controls at low prediction errors suggesting that learning is otherwise equivalent between groups. Moreover, number of points garnered between groups across the task was comparable. Hence, it is more probable that uncertainty and/or not-just-right perceptions are driving this unique behaviour in the adolescents with OCD.

5.5.2 Blunted confidence updating in OCD

Next, confidence ratings in the adolescent OCD group were found to be insensitive to the influence of prediction errors, while controls decreased their confidence ratings when predictions errors were high. This finding is reminiscent of recent dimensional psychiatry work revealing a relationship between compulsive behaviour/intrusive thoughts and inflated confidence levels in healthy adults who completed a perceptual decision-making task (Rouault, Seow, Gillan, & Fleming, 2018), and an online version of the predictive-inference task (Seow & Gillan, 2020). Furthermore, in the latter study confidence updating in compulsive participants was less influenced by unexpected outcomes and feedback, similar to what was found in my study.

Blunted confidence updating in patients supports the proposal by Fradkin, Adams et al. (2020) that individuals with OCD do not use external evidence to inform their beliefs and actions. Beliefs may instead be influenced by an intrinsic sense of 'wrongness' (akin to the 'alarm' analogy used earlier). Indeed, patients with OCD on this task appear to be behaving in accordance with their own volition and not according to the task structure, by updating their choices when it is not necessary, and not updating their confidence levels when they are expected to do so.

By contrast, healthy controls updated their confidence according to prediction errors, which aligns with prior work demonstrating that healthy adolescents adjust their behaviour more following negative prediction errors compared to adults (Hauser, Iannaccone, Walitza, Brandeis, & Brem, 2015). This demonstrates a pattern of emerging evidence where typically developing adolescents actually seem to be punishment averse, and not reward sensitive as was previously thought, on reinforcement learning paradigms compared to other age groups (Rosenbaum, Grassie, & Hartley, 2020). Inversely, adolescents with OCD do not take into account external feedback when updating confidence, and thus appear less affected by negative feedback compared to healthy adolescents.

5.5.3 No difference in confidence-action coupling between OCD and healthy adolescents

Despite numerous studies demonstrating a belief-action dissociation in adult OCD and even in healthy adults with compulsive tendencies (Hauser, Allen, et al., 2017; Rouault et al., 2018; Seow, O'Connell, & Gillan, 2020; Vaghi et al., 2019), I found no difference between adolescent patients and controls when formally testing the strength of association between action and confidence in my sample of participants. This null result was in spite of observing unusual patterns of action and confidence updating in the OCD group. Nonetheless, excessive action updating by patients was only seen in specific circumstances (following low prediction errors), which may the reason for not seeing an overall confidence-action dissociation in OCD across the entire task.

At first glance, it appears that adolescents with OCD more often than not update their confidence and actions in parallel, unlike adults with the disorder. This suggests that the two constructs (confidence and action) become unlinked over time, perhaps as disease duration increases and heavily impacts executive functioning. However, I propose an alternative explanation: meta-cognition may still be developing in healthy adolescents resulting in a lack of noticeable differences between patients and controls. This is supported by research demonstrating that accurate meta-cognition only begins to emerge in early adolescence but strengthens over time well into late adolescence before plateauing in adulthood (Fandakova et al., 2020; Moses-Payne, Habicht, Bowler, Steinbeis, & Hauser, 2020; Weil et al., 2013). Likewise, an impressive new piece of computational research by Jepma, Schaaf, Visser, & Huizenga (2020) has discovered that that healthy adolescents, compared to healthy adults, overestimated the importance of recent volatile feedback rather than take into account information accumulated across the task so far. Crucially, self-reported certainty did not differ between age agroups, highly indicative of a mismatch between confidence and behaviour. In short, adolescents in Jepma et al.'s study were behaving similar to adult OCD patients in Vaghi, Luyckx et al.'s (2017) predictive-inference study. In my current study, detecting an effect of OCD is difficult as the adolescent control group are likely to also update action and confidence independently. The adolescent controls will eventually develop into adults who can make more accurate judgements of their own performance in the face of environmental volatility, while adolescents with OCD will unfortunately continue to grapple with this deficit throughout their lives (as shown in Vaghi et al.'s study where the action-confidence dissociation was highly pronounced in the adults with OCD but not healthy adults).

5.5.4 Medication effects

Nonetheless, the future may not be as bleak as was just implied for youths with OCD as I have found that excessive updating during low prediction errors was primarily driven by unmedicated patients with OCD, while patients medicated with SSRIs did not differ significantly from controls (which is at odds with findings from previous chapters in this thesis). This is in contrast to Vaghi, Luyckx et al.'s findings where medication dosage in their OCD sample did not predict increased learning rates, although Vaghi, Luyckx et al. did not have enough non-medicated subjects in their OCD sample to conduct a group analysis. One interpretation could be that symptoms of OCD in younger people are more amenable to treatment compared to adults who likely also have longer disease durations. Indeed, it was found that juvenile patients respond faster to pharmacological and therapeutic treatment compared to adults (Mancebo et al., 2008). Thus, SSRIs seem to be ameliorating compulsive tracking of the coin by adolescent patients on the task.

This also somewhat aligns with research suggesting that medicated adult patients show superior performance to medication-naïve patients on various learning and planning tasks (Lochner et al., 2020; Palminteri et al., 2012). Importantly, SSRIs administered to adolescents and children with OCD have been found to lead to significant improvements on verbal memory, processing speed, inhibition, and cognitive flexibility compared to baseline (Andrés et al., 2008). However, these results contrast with previous chapters of this thesis that show more abnormal decision-making in medicated adolescent patients. Medication effects are discussed further in Chapter 7.

5.5.5 Limitations and Further Research

As has become a running theme in this thesis, it is important to highlight that the OCD group's sample size, particularly after further separating the group by medication status, is still quite limited and caution should be exercised when interpreting the results.

Next, I did not consider other models when fitting behaviour aside from the quasi-optimal Bayesian learning model that had been previously used and validated by Vaghi, Luyckx et al. (2017) for this task. While the model in question was found to be the best-fitting one for adult behaviour, it may be less suitable for capturing and disentangling adolescent behaviour. Jepma et al. (2020) found that distinct reinforcement learning models best fit their adult and adolescent subgroups, where a model with dynamic learning rates was more suitable for the adult data and a model with a single learning rate across the entire task better fit the adolescent data. Different families of models for this task may be considered in the future.

Lastly, it is important to note that although I find it plausible that healthy adolescents showed age-related action-confidence discoupling (which is why we see no differences on this compared to adolescent patients) this was not formally tested. Moreover, no association between age and action-confidence coupling strength was found in this sample. Hence, in an upcoming study I aim to combine my dataset with Vaghi, Luyckx et al.'s (2017) adult dataset to investigate whether the presence of OCD and age interact to influence action-confidence coupling.

5.5.6 Conclusion

Inspired by previous work detailing a novel action-outcome dissociation in adults with OCD, I demonstrated that adolescents with OCD do not show such a marked dissociation compared to healthy matched controls. This finding may be driven by meta-cognition not being fully developed in the healthy adolescent group, and I hope to formally probe the possibility for these processes being age-dependent in a future study. Instead, patients with OCD deviated most from healthy adolescent behaviour when experiencing low magnitude prediction errors whereby they made frequent

unnecessary updates of the bucket location. Furthermore, patients' confidence ratings were not as influenced by prediction errors as those of control participants. I posit that youths with OCD update their actions and beliefs according to their own internal sensations of uncertainty rather than following observable changes in the task environment. This is consistent with an amalgamation of prior research reporting uncertainty-driven information sampling and checking, error-related negativity, and blunted confidence updating in obsessive-compulsive individuals. I also provide preliminary evidence for aberrant action-updating to be remediated by SSRI treatment in youths with OCD, emphasising the importance of early intervention in improving disorder related decision-making deficits.

Chapter 6: Probabilistic Reversal Learning in Adolescents with OCD

6.1 Introduction

As described in Chapter 1 of this thesis, reversal learning involves the adaptation of behaviour according to changes in stimulus-reward contingencies (Rolls, 1999). Probabilistic reversal learning has an added layer of complexity as the feedback given is probabilistic, meaning one has to distinguish between veridical (true) and spurious (false) feedback in order to make optimal choices (Cools, Clark, Owen, & Robbins, 2002; Swainson et al., 2000). The paradigm is commonly used to assess domains of cognitive flexibility and feedback learning. Deficits in probabilistic reversal learning have been found in a variety of psychiatric groups including schizophrenia, Parkinson's disease, major depressive disorder, anxiety disorders, and OCD (Dickstein et al., 2010; Peterson et al., 2009; Remijnse et al., 2009; Remijnse et al., 2006; Robinson, Cools, Carlisi, Sahakian, & Drevets, 2012; Tavares et al., 2008; Waltz & Gold, 2007). Due to this lack of specificity, research is increasingly employing computational methods to understand latent cognitive processes unique to populations with different psychiatric conditions. Findings from such methods in the context of OCD are described later in this section.

First, the majority of studies have sought to understand probabilistic reversal learning in patients with OCD using a combination of standard statistical methods and neuroimaging, although such studies report varied results. One study by Remijnse et al. (2006) reported that adults with OCD displayed more spontaneous errors and fewer correct responses overall compared to matched controls. Moreover, differential brain activity to punishment and reward processing was found; patients under-recruited the right medial and lateral OFC, and right caudate nucleus during reward processing and showed decreased activity in the left posterior OFC, bilateral insula, bilateral anterior PFC, and bilateral dlPFC during punishment processing. Additionally, Morein-Zamir et al., (2014) found that adult OCD patients with hoarding tendencies showed impaired performance on the task following reversal. Likewise, a more recent study by Tezcan, Tumkaya, & Bora (2017) showed that adults with OCD and their unaffected first-degree relatives make more reversal errors compared to controls. In addition, adults with OCD also reportedly show a bias towards avoidance learning as they are more likely to avoid stimuli associated with negative outcomes compared to preferring stimuli associated with positive outcomes (Endrass et al., 2011). Moreover, a meta-analysis probing measures of flexibility across various cognitive tasks including the probabilistic reversal learning task reported that OCD patients tend to show more shifts after probabilistic negative feedback and

make more errors before reversals compared to control subjects (Fradkin et al., 2018). On the whole, these results indicate impaired reversal learning and oversensitivity to punishing feedback in adults with OCD.

However, a proportion of the samples in Reminjnse et al.'s (2006) and Endrass et al.,'s (2011) studies had comorbid depressive disorder alongside OCD which may have influenced the results. In fact, Reminjse et al. (2009) attempted to replicate the original Remijnse et al. (2006) study with participants who only had a diagnosis of OCD and found no behavioural deficits on probabilistic reversal learning. Other studies also report a lack of OCD-related behavioural impairments on the task (Chamberlain, Fineberg, Blackwell, et al., 2007; Ersche et al., 2011; Valerius et al., 2008). Nevertheless, altered brain activity in adults with OCD in response to the task seems to be a robust finding, as Reminjse et al. (2009) found right medial OFC underactivation linked to reward processing similar to the original 2006 study.

Incidentally, research has also uncovered possible influences of serotonin on probabilistic reversal learning, which is of relevance to OCD as patients are normally medicated with SSRIs. On the one hand, depletion of tryptophan (a protein that promotes serotonin synthesis) for acute periods in healthy subjects leads to slower response times during probabilistic reversal learning (Murphy et al., 2002). Inversely, tryptophan depletion has also been demonstrated to impair deterministic reversal learning (Kanen, Apergis-Schoute, et al., 2020) but not probabilistic reversal learning (Kanen, Arntz, et al., 2020). Contrasting with these findings, acute SSRIs (which should increase serotonin availability in the brain) administered to healthy adults was found to impair probabilistic reversal learning (Chamberlain, Müller, et al., 2006; Skandali et al., 2018). More recently, Apergis-Schoute et al. (in-prep) demonstrated that adults with OCD medicated with SSRIs were especially impaired at acquisition (pre-reversal) learning on the probabilistic reversal learning task, while unmedicated adult patients were impaired at deterministic reversal learning under punishment conditions. While these findings are highly varied, they overall suggest dissociable effects of serotonin on probabilistic and deterministic reversal learning. In the context of adult OCD, it appears that serotonergic medication promotes learning deficits during probabilistic reversal learning.

Presently, studies are utilising computational modelling to disentangle behavioural strategies on the task as findings obtained from standard analyses are highly heterogeneous. Hitherto, three studies fitting reinforcement learning models to task data have found reduced choice perseveration and increased exploratory decision-making on the task in patients with OCD (Apergis-Schoute et al., in-preparation; Hauser et al., 2017; Kanen et al., 2019). Hauser et al. (2017) propose decreased

perseveration may reflect a form of checking behaviour wherein patients feel the need to check the non-optimal stimulus to ascertain that it is indeed delivering the predicted feedback. This explanation fits a framework of OCD postulated by Fradkin, Adams et al. (2020) where patients with OCD are unable to rely on prior accumulated information (feedback acquired throughout the duration of the task) to reduce their uncertainty about the value associated with each stimulus, and turn to exploratory/checking behaviour as a consequence. Reduced perseveration and increased exploration appear to be characteristics specific to OCD as computational modelling of data from populations with anxiety and depression reveal altered feedback processing but no abnormalities in exploration or perseveration (Brolsma et al., 2020; Lighthall, Gorlick, Schoeke, Frank, & Mather, 2013; Mather & Lighthall, 2012; Ting et al., 2020).

No research yet has conducted computational modelling of the probabilistic reversal learning task data extracted from a large sample of adolescents with OCD. Hauser et al. (2017)'s sample included both adolescents (n=22) and adults (n=10) with OCD, and the authors conducted comparative analyses between the two age-groups and initially found that adolescent patients displayed a lower perseveration parameter value than adult patients. However, this difference ceased to be significant after controlling for age and intelligence. Hauser et al.'s study provides preliminary evidence that adolescents with OCD display somewhat equivalent behaviour to their adult counterparts but larger sample sizes in each group are necessary to draw firm conclusions. Other decision-making studies have indeed produced results suggestive of lower perseveration in young patients, for example on the Iowa Gambling task, children with OCD make more disadvantageous choices and spend more time exploring non-optimal decks than healthy children (Kodaira et al., 2012; Norman et al., 2018).

To disentangle mechanisms underlying learning and decision-making in adolescent OCD, a probabilistic reversal learning task was administered to a large sample of adolescent participants (50 patients and 53 controls). I used a Bayesian hierarchical modelling approach to assess trial-by-trial task data. Five models with different combinations of parameters were fitted to the data and compared. It was predicted that adolescents with OCD would show reduced perseveration and more exploratory decision-making compared to controls matched for age, gender, and IQ, which aligns with research studying adults with the disorder. As non-modelling results of probabilistic reversal learning in OCD vary between studies, no specific hypotheses were formulated for the frequentist statistical analyses portion of this current study. Nonetheless, I chose task measures that enabled testing of competing cognitive theories of OCD, namely related to feedback sensitivity and perseveration. In addition, as past research has identified possible effects of serotonergic medication on probabilistic reversal learning, I also observed the effects of SSRIs on patient performance.

6.2 Methods

6.2.1 Sample

Initially, 20 adolescents with OCD and 21 healthy controls completed the probabilistic reversal learning task outlined in this chapter. However, it was later discovered that the same task had been administered to 32 adolescents with OCD and 32 healthy adolescents in an earlier PhD project completed by Dr. Julia Gottwald in 2017. After obtaining Dr. Gottwald's permission, I was able to combine our datasets. It should also be noted that Dr. Gottwald had not yet published this data, and the data were analysed in her PhD in a very different way from the analysis conducted in this current chapter (i.e. computational modelling had not been conducted on this dataset until now). In addition, the inclusion and exclusion criteria Dr. Gottwald used to recruit participants were identical to the criteria I have used for my data collection, allowing for our datasets to be easily amalgamated. After removing 2 subjects with OCD from Dr. Gottwald's dataset, as they had also been recruited for my study, I achieved a final sample size of 50 adolescents with OCD and 53 control subjects. Thirty adolescents with OCD were receiving SSRI medication at the time of completing the task while 20 were medication-naïve. Out of the 30 patients receiving medication, 20 were medicated with sertraline and 10 were medicated with fluoxetine. The mean dosage was 96.17mg (std dev: 62.75mg) and the dose ranged from 20mg to 200 mg. Digit span and IQ data is missing from one OCD participant from my original sample of 20 adolescents with OCD. Also, Dr. Gottwald did not administer the digit span test to her sample of participants. Hence, digit span data is only available for 19 OCD patients and 21 controls. Further demographic details are outlined in the Results section of this chapter.

6.2.2 Probabilistic Reversal Learning Task

The paradigm used here is identical to the task originally used by Murphy, Smith, Cowen, Robbins, & Sahakian (2002). Participants were shown two stimuli, composed of four red and four green lines, on screen (see Figure 6.1). They were instructed to choose either stimuli on every trial by touching it on a laptop screen. The following written instructions were provided before the task began:

"On the screen there are two patterns, one red and one green. On each go, you must choose one of these colours and the computer will tell you whether your choice is correct or wrong. Each colour will sometimes be correct and sometimes be wrong, but one of the colours will tend to be correct more often than the other. What you have to do is find out which colour is usually correct, choose that colour every time, and stick with it even if it is occasionally wrong. At some point the rule may

change so that the other colour is usually correct, in which case you should choose that one every time."

The task consisted of 80 trials in total and was split into Acquisition and Reversal phases, each consisting of 40 trials. The Acquisition phase required participants to discriminate between the optimal and non-optimal stimuli. The optimal stimulus was programmed to provide positive feedback ('Correct') on 80% of trials and negative feedback ('Incorrect') on 20% of trials. The non-optimal stimulus was programmed to provide negative feedback on 80% of trials and positive feedback on 20% of trials. The stimulus chosen by participants on the first trial was assigned as the optimal stimulus for the rest of the Acquisition phase. Subsequently during the Reversal phase, the positive to negative feedback ratio associated with each stimulus was reversed. In other words, the stimulus that was previously optimal became non-optimal and *vice versa* – see Figure 6.2 for a schematic of the feedback contingencies associated with each stimulus. Participants were not cued when the reversal occurred.

On correct trials, the word 'Correct' would be displayed in green alongside a consonant tone, whereas on incorrect trials, the word 'Incorrect' would be displayed in red alongside a dissonant tone. There was no time limit for responding in each trial. The task duration was approximately 7 minutes in total.

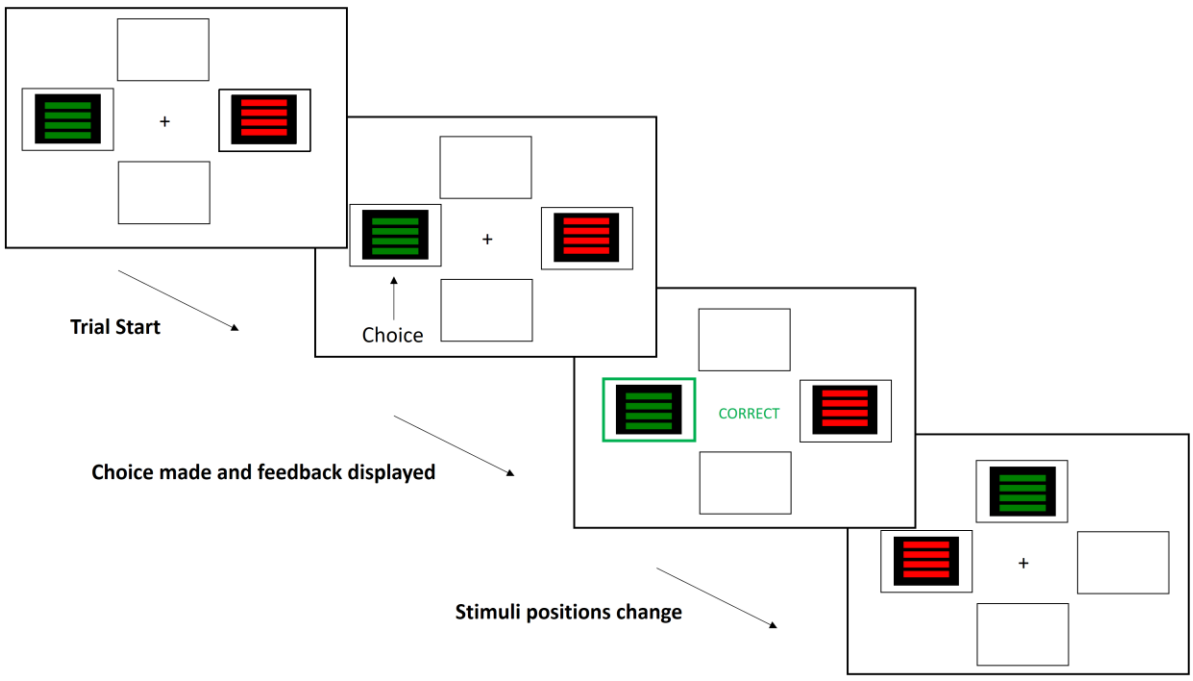

FIGURE 6.1: STIMULUS PRESENTATION IN THE PROBABILISTIC REVERSAL LEARNING TASK

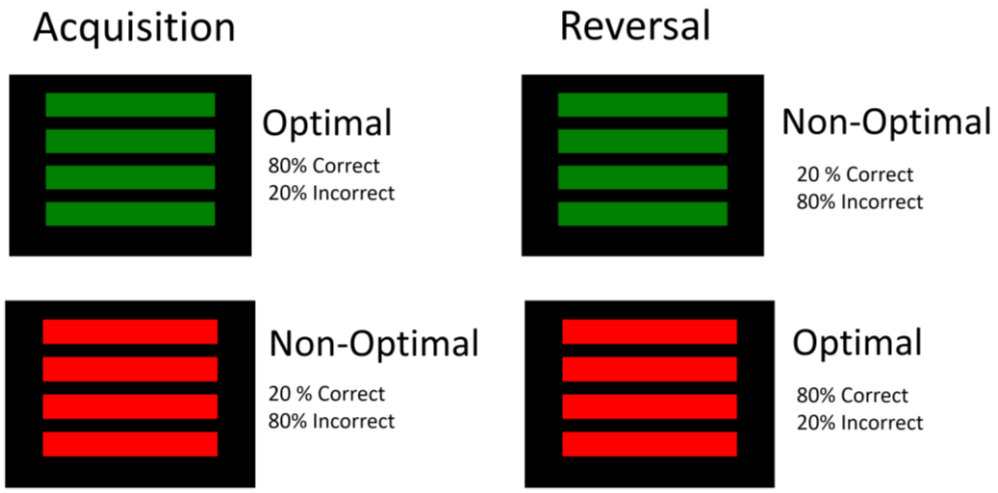

FIGURE 6.2: FEEDBACK CONTINGENCIES ASSOCIATED WITH EACH STIMULUS IN THE ACQUISITION AND REVERSAL PHASES.

6.3 Statistical Analyses

6.3.1 Standard analyses

Data cleaning and statistical analyses were conducted in Matlab R2017b and RStudio 3.5.0.

The following 5 outcome measures were analysed: proportion of perseverative errors (number of perseverative responses made in a row immediately following reversal), probability of correct responses, probability of switching following spurious negative feedback (SNF), probability of staying following veridical positive feedback (VPF) (identical measures were used in Skandali et al. (2018) and Kanen, Arntz, et al. (2020)), and mean reaction time. Probabilities of switching following SNF and staying following VPF were calculated by counting the number of times each participant switched following SNF and stayed following VPF, and dividing these values by the number of times participants had the opportunity to carry out these switching and staying behaviours. Mixed-level regressions were conducted using the lmer function from the lme4 R package (Bates et al., 2014) to assess the effects of Group (OCD vs CTL) and Phase (pre-reversal vs post-reversal) on the outcome measures. The model for the proportion of perseverative errors did not include Phase as an independent variable as the measure only looked at perseverative responses in the reversal phase. The regression analyses were repeated but this time Z-scored ages, IQ scores, and gender were added as covariates to control for these possible confounding variables.

Through inspecting the data and generating QQplots of residuals, it was found that many model residuals were not normally distributed as a result of outliers in the data. To rectify this, robust mixed regressions were implemented for some models instead using the rlmer function from the "robustlmm" R package (Koller, 2016). The robust mixed regression is similar in principle to a mixed linear regression, except it reduces the weights of outlier values enabling robust coefficient estimates to be obtained. P-values to assess significance were calculated using Satterthwaite approximations of degrees of freedom and robust standard errors, a method which has been conducted in other studies (Geniole et al., 2019; Luke, 2017). To control for multiple comparisons, p-values were adjusted according to the Benjamini-Hochberg procedure (Benjamini & Hochberg, 1995) using the 'p.adjust' function in base R.

The analyses were then re-run, this time exploring the effects of medication on dependent measures. The OCD group was divided into MED- and MED+. To analyse task measures, mixed-linear and mixed-robust regressions were implemented once more. Pairwise comparisons for Group-by-Phase interactions were performed using post-hoc Wilcoxon tests with Bonferroni correction. Magnitude of an effect was determined via a Wilcoxon effect size (Wilcoxon r) calculated by dividing the test z-statistic by the square root of the sample size ($Z/\sqrt{N}$). The following interpretations of effect size values were used, small effect: 0.10 - < 0.3, moderate effect: 0.30 - < 0.5 and large effect: >= 0.5.

Pearson correlations were conducted to quantify the relationships between task measures and demographic-intelligence-clinical measures (age, IQ, digit span, OCI, BDI, and BAI scores).

6.3.2 Computational Modelling

To understand latent processes underlying learning and decision-making on this task, a family of reinforcement learning (RL) models were fitted to data using hierarchical Bayesian methods. Model code was adapted from Kanen et al. (2019). In total, five hierarchical RL models were fitted to data.

Model 1

Model 1 served to discern whether a simple RL model with two parameters best described the data and accounted for differences between groups. The model comprised a learning rate parameter (α) and a reinforcement sensitivity parameter (τ). A value function (Q_t) was assigned to each task stimulus denoting the expected rewards associated with them. On every trial (t), the value of free learning rate parameter α determined the extent to which Q_t assigned to stimulus k on trial t is updated following an outcome (R) received after choosing a stimulus. Concretely, this was done according to the Rescorla-Wagner rule:

$Q_{k,t+1} = Q_{k,t} + \alpha(R_t - Q_{k,t})$ – Equation 6.1

R would equal 1 following rewarded outcomes, and 0 following unrewarded outcomes. The term $R_t - Q_{k,t}$ represents the prediction error. Values of α closer to 1 indicate faster adaptations of $Q_{k,t}$ according to the prediction error term, while lower values of α indicate slower adaptations.

τ (reinforcement sensitivity) is essentially an inverse temperature parameter associated with the value functions assigned to each stimuli. This parameter was plugged into a softmax rule which was used to determine the probability (p) of choosing a stimulus k on trial t:

$p_{k,t} = \frac{\exp(\tau Q_{k,t})}{\sum_{i=1}^{k} \exp(\tau Q_{i,t})}$ – Equation 6.2

τ determined the extent to which participants' actions were driven by the value functions associated with the chosen stimulus. A high τ leads to more exploitative behaviour whereby a participant chooses to mostly maximise their rewards. A low τ enables more exploratory behaviour.

Model 2

Model 2 was as Model 1 except separate α were implemented to account for rewarding and punishing outcomes:

$Q_{k,t+1} = Q_{k,t} + \alpha_{rew}(R_t - Q_{k,t})$ – if $R = 1$ – Equation 6.3

$Q_{k,t+1} = Q_{k,t} + \alpha_{pun}(R_t - Q_{k,t})$ – if $R = 0$ – Equation 6.4

This was done to examine differences in learning from reward and from punishment and to test the theory that patients with OCD are more sensitive to punishment. Hence, this model contained 3 free parameters, α_{rew}, α_{pun}, and τ.

Model 3

Model 3 was similar to Model 2 but with the addition of τ_{stim} (stimulus stickiness), which is an inverse temperature parameter that reflects the tendency of a participant to respond to the same stimulus chosen in a previous trial. High values of τ_{stim} denote increased tendency to 'stick' to a choice while low values denote a tendency to switch away from the choice. The aim of including this parameter was to test the presence of repetitive responding in adolescents with OCD. This parameter was added to the softmax function as follows:

$$p_{k,t} = \frac{\exp(\tau Q_{k,t} + \tau_{stim}\, s_{k,t-1})}{\sum_{i=1}^{k} \exp(\tau Q_{i,t} + \tau_{stim}\, s_{i,t-1})}$$ – Equation 6.5

S represents whether one of the stimuli (in this case stimulus 1) was chosen or not (S = 1 if chosen; S = 0 if not). Thus, this model contained 4 parameters in total α_{rew}, α_{pun}, τ, and τ_{stim}.

Model 4

Model 4 was as Model 3 but with 3 parameters (α, τ, τ_{stim}) as it contained a single learning rate controlling the adaptation of the value functions.

Model 5

Model 5 was distinct from the aforementioned models. It was an experience-weighted attraction (EWA) model previously used by den Ouden et al. (2013). It contains 3 free parameters: φ (phi), ρ (rho), and β (beta).

The model served to decouple acquisition (pre-reversal) and reversal via the experience decay factor parameter ρ that enables the balance between past experience and new information to increasingly tip in favour of past experiences. The 'experience weight' of a current choice ($n_{c,t}$), which reflects how often a stimulus has been chosen, is updated according to ρ:

$n_{c,t} \leftarrow n_{c,t-1}\, \rho + 1$ – Equation 6.6

The intuition behind ρ is that over time experience accumulated during acquisition could make reversal more difficult leading to perseveration. ρ was allowed to range between 0 and 1. When ρ = 0, predictions are always driven by most recent outcomes, whereas when ρ = 1 all trials are weighted equally leading to more sluggish reversal.

The value of a choice on every trial, $v_{c,t}$, is updated according to the outcome, λ, and the pay-off decay factor φ, which is equivalent to the learning rate in the Rescorla-Wagner model.

$v_{c,t} \leftarrow (v_{c,t-1}\, \varphi\, n_{c,t-1} + \lambda_{t-1}) \,/\, n_{c,t}$ – Equation 6.7

When $\rho = 0$, $n_{c,t}$ on every trial becomes 1 as per Equation 6.6, and therefore Equation 6.7 reduces to a standard Rescorla-Wagner model.

Similar to models described earlier, probability of choices, P, is determined by a softmax process

$$P(c_{t+1} = i) = \frac{e^{\beta V(c=i,t+1)}}{\sum_j e^{\beta V(c=j,t+1)}}$$ – Equation 6.8

Where the inverse temperature parameter, *β,* is allowed to vary.

Priors

Each model parameter was drawn from a group level distribution separate for OCD and CTL. Inter-subject variability for each parameter was sampled from half-normal prior distributions, enabling estimates to be constrained to be positive. Individual subject parameters were sampled from normal distributions whose means were the group level parameter values and whose variances were from the inter-subject variability parameter values.

Group-level parameters were sampled from the following prior distributions:

$\alpha_{group}, \alpha_{group,rew}, \alpha_{group,pun}, \varphi_{group}, \rho_{group} \sim \text{Beta}\ (1.2,1.2)$

$\tau_{group}, \beta_{group} \sim \text{Gamma}\ (4.82,0.88)$

$\tau_{group,stim} \sim \text{Normal}(0,1)$

Prior distributions over the inter-subject variability, σ, in the model parameters were as follows:

$\sigma_{\alpha}, \sigma_{\alpha\text{-}rew}, \sigma_{\alpha\text{-}pun}, \sigma\tau_{\text{-}stim}, \sigma_{\varphi}, \sigma_{\rho} \sim \text{half-Normal}(0,0.05)$

$\sigma\tau, \sigma_{\beta} \sim \text{half-Normal}(0,1)$

Where half-Normal is the normal distribution constrained to positive values.

Subject specific parameter values were generated from group-level parameters and inter-subject variability parameters, for example, in the case of α_{rew}:

$\alpha_{rew,subject} = \alpha_{rew,group(subject)} + \sigma_{\alpha rew(subject)}$ – Equation 6.9

Model Fitting and Comparison

All models were fitted to data using MCMC sampling implemented in Stan v. 2.21.1. Eight randomly-initialised MCMC chains were used. Convergence was checked using the potential scale reduction statistic $\widehat{R}$. A cut-off $\widehat{R}$ value of 1.2 (also used in Kanen et al., 2019) was used to check that the chains were well-mixed for each parameter .

Models were compared using a bridge sampling estimate of the marginal likelihood via the "bridgesampling" R package (Gronau et al., 2017). This method directly estimates the marginal

likelihood and penalises the number of free parameters in a model, which helps guard against overfitting.

Parameter Recovery

Parameter recovery was conducted to verify the validity of the winning model and that parameter values were meaningful (and not occurring by chance) (Wilson & Collins, 2019). The winning model was first used to simulate synthetic data from 100 'participants'. The free parameters were replaced with the mean fitted parameter values per group estimated from the actual human data. I then ascertained whether the true parameter values could be recovered by fitting the winning model to the simulated data, and checking whether the true and generated parameter values fell within their corresponding 95% HDI. This same method for parameter recovery was conducted by Apergis-Schoute et al. (in-prep).

6.4 Results

6.4.1 Standard Analyses (CTL vs OCD)

Demographic, intelligence, and clinical scores for CTL and OCD are summarised in Table 6.1. The groups were well-matched for age, gender, IQ, and digit span scores. However, OCD showed significantly increased depression, anxiety, and obsessive-compulsive ratings.

Table 6.1: Mean scores and standard deviations per group and statistical tests.

	CTL (n = 53)	**OCD (n = 50)**	**STATISTIC**
GENDER (F:M)	30/23	29/21	$\chi 2$ (1)=0.02; p=.89
AGE	16.38 ± 2.05	16.57 ± 1.75	Z =-0.28; p=.78
WASI-II (IQ)[a]	109.11 ± 10.79	106.57 ± 12.10	t(100) = 1.22, p=.27
BDI**	46.81 ± 6.43	59.32 ± 10.76	t(79.14) =-7.11; p=4.59e-10
BAI**	48.04 ± 7.09	62.82 ± 11.29	t(81.59) = -7.91; p=1.10e-11
OCI**	9.25 ± 6.56	29.16 ± 12.83	Z =-7.56; p=4.10e-14
Y-BOCS	N/A	23.47 ± 5.14	N/A

Digit Span (Forwards) [b]	10.81 ± 2.79	11.21 ± 2.44	Z= -0.26; *p*=.79
Digit Span (Backwards) [b]	8.33 ± 2.15	8.05 ± 1.87	t(38)= 0.44; *p*=.66

Key- CTL: Control Group; OCD: Obsessive-Compulsive Disorder group; WASI-II: Wecshler's Abbreviated Intelligence Scale – IV; IQ: Intelligence Quotient; BDI: Beck's Depression Inventory (t-scored); BAI: Beck's Anxiety Inventory (t-scored); OCI: Obsessive-Compulsive Inventory; CY-BOCS: Children's Yale-Brown Obsessive-Compulsive Scale. *p<.05; **p<.01, [a] missing data from one OCD participant; [b] only included 21 CTL and 19 OCD.

Summary statistics and results of task measures from the probabilistic reversal learning task are summarised in Table 6.2 and Figure 6.3. In brief, there was a significant Group (OCD, CTL)-by-Phase (Acquisition, Reversal) interaction for the proportion correct (Coefficient estimate = -0.13, $t(101) = -4.52$, $p = .000068$) and proportion staying following VPF (Coefficient estimate = -0.075, $t(101) = -3.24$, $p = .0032$) measures. This indicates that during reversal, OCD made less correct responses overall and also stayed less following veracious positive feedback. No group effects for all other measures were detected. There was a significant effect of Phase over proportion correct (Coefficient estimate = -0.11, $t(101) = -5.69$, $p = 4.80e\text{-}6$), wherein participants tended to make fewer correct responses during the reversal phase.

Table 6.2: Summary statistics and results from mixed linear regressions and robust mixed regressions. Mean and standard deviations per group (CTL, OCD) and per phase (Acquisition, Reversal) are reported. Wald's 95% confidence intervals were calculated. p(perseverative errors) has a separate section as different tests (robust linear regression and robust F-test) were used to analyse this measure. Significant variables and corresponding p-values are in bold.

	ACQUISITION		REVERSAL									
Dependent Variable	**CTL (M±SD)**	**OCD (M±SD)**	**CTL (M±SD)**	**OCD (M±SD)**	**Independent Variable**	**Coefficient Estimate**	**Statistic (t)**	**df**	**BH adjusted p-value**	**2.5% CI**	**97.5% CI**	**SE**	**Test used**
p(Correct)	0.96 ± 0.11	0.94 ± 0.097	0.83 ± 0.16	0.61 ± 0.31	Group	-0.024	-1.17	101	.24	-0.063	0.016	0.020	Robust Mixed Model
					Phase	-0.11	-5.69	101	**.0000048**	-0.15	-0.074	0.020	
					Group x Phase	-0.13	-4.52	101	**.000068**	-0.18	-0.073	0.029	
RT	1035.92 ± 401.98	1129.45 ± 428.97	975.41 ± 355.06	1000.84 ± 308.71	Group	93.52	1.26	118.75	.21	-51.72	238.77	74.24	Mixed Linear Model
					Phase	-60.52	-2.05	101	.086	-118.32	-2.73	29.50	
					Group x Phase	-68.09	-1.61	101	.15	-151.05	14.87	42.35	
p(Switching following SNF)	0.065 ± 0.14	0.094 ± 0.21	0.12 ± 0.16	0.27 ± 0.34	Group	0.033	1.20	101	.23	-0.021	0.088	0.028	Robust Mixed Model
					Phase	0.024	0.86	101	.39	-0.030	0.077	0.027	
					Group x Phase	0.037	0.94	101	.35	-0.040	0.11	0.040	
p(Staying following VPF)	0.97 ± 0.098	0.95 ± 0.081	0.93 ± 0.17	0.73 ± 0.34	Group	-0.022	-1.34	101	.18	-0.054	0.010	0.016	Robust Mixed Model
					Phase	-0.017	-1.05	101	.39	-0.048	0.015	0.0161	
					Group x Phase	-0.075	-3.24	101	**.0032**	-0.12	-0.030	0.023	
Dependent Variable			**CTL (M±SD)**	**OCD (M±SD)**	**Independent Variable**	**Coefficient Estimate**	**Robust F statistic**	**df**	**p-value (from robust F test)**	**2.5% CI**	**97.5% CI**	**SE**	**Test Used**
p(Perseverative Error)			0.11 ± 0.13	0.21 ± 0.27	Group	0.021	2.13	1,101	.15	-0.00700	0.048	0.014	Robust Linear Model

Key- CTL: Control group; OCD: Patient group; M: mean; SD: standard deviation; df: degrees of freedom; BH: Benjamini-Hochberg Correction; CI: confidence interval; SE: regression standard error; p(Correct): proportion correct choices; mean RT: reaction time; p(Switching following SNF): proportion of switching in response to spurious (false) negative feedback; p(Staying following VPF): proportion of staying in response to veracious (true) positive feedback; p(Perseverative Error): proportion of perseverative errors (only during reversal phase).

The analyses were then repeated controlling for age, gender, and IQ. These results are summarised in Table 6.3. The Group-by-Phase interaction for proportion of correct responses and proportion of staying to VPF remained significant after controlling for these variables. IQ had a significant effect over proportion correct (Coefficient estimate = 0.0023, $t(97) = 3.53$, $p = .0027$), proportion of switching following SNF (Coefficient estimate = -0.002, $t(97) = -2.57$, $p = .020$), and proportion of staying following VPF (Coefficient estimate = -0.0016, $t(97) = -3.22$, $p = .0045$). In other words, participants with higher IQ made more correct responses, and repeated choices more following both VPF and SNF.

Table 6.3: Summary statistics and results from mixed linear regressions and robust mixed regressions. Age, IQ, and gender were added to the models as nuisance regressors. Mean and standard deviations per group (CTL, OCD) and per phase (Acquisition, Reversal) are reported. Wald's 95% confidence intervals were calculated. p(perseverative errors) has a separate section as different tests (robust linear regression and robust F-test) were used to analyse this measure. Significant variables and corresponding p-values are in bold.

Dependent Variable	**Independent Variable**	**Estimate**	**Statistic (t)**	**df**	**BH adjusted p-value**	**2.5% CI**	**97.5% CI**	**SE**	**Test used**
p(Correct)	Age	0.010	1.34	97	.48	-0.0048	0.026	0.0077	Robust Mixed Model
	Gender	-0.032	-2.04	97	.11	-0.062	-0.0012	0.016	
	IQ	0.0023	3.53	97	**.0027**	0.0011	0.0037	0.00068	
	Group	-0.021	-0.99	97	.32	-0.064	0.021	0.022	
	Phase	-0.12	-5.57	97	**.00000034**	-0.16	-0.076	0.021	
	Group x Phase	-0.14	-4.49	97	**.000048**	-0.20	-0.077	0.031	
RT	Age	13.24	0.36	97	.86	-57.23	83.71	36.52	Mixed Linear Model
	Gender	31.66	0.43	97	.67	-110.50	173.82	73.68	
	IQ	-5.30	-1.66	97	.13	-11.44	0.85	3.19	
	Group	82.04	1.09	113.572	.32	-63.72	227.80	75.56	
	Phase	-60.53	-2.05	100	.086	-118.24	-2.80	29.46	
	Group x Phase	-73.02	-1.72	100	.12	-156.29	10.26	42.51	
p(Switching following SNF)	Age	-0.013	-1.31	97	.48	-0.032	0.0063	0.0097	Robust Mixed Model
	Gender	-0.015	-0.77	97	.56	-0.053	0.023	0.020	
	IQ	-0.0022	-2.57	97	**.02**	-0.0038	-0.00051	0.00085	
	Group	0.030	1.11	97	.32	-0.023	0.083	0.027	
	Phase	0.024	0.92	97	.36	-0.028	0.076	0.027	
	Group x Phase	0.031	0.82	97	.41	-0.044	0.11	0.038	
p(Staying following VPF)	Age	0.0062	1.07	97	.48	-0.0051	0.017	0.0058	Robust Mixed Model
	Gender	-0.021	-1.84	97	.12	-0.044	0.0014	0.012	
	IQ	0.0016	3.22	97	**.0045**	0.00063	0.0026	0.00050	
	Group	-0.018	-1.11	97	.32	-0.050	0.014	0.016	
	Phase	-0.017	-1.09	97	.36	-0.048	0.014	0.016	
	Group x Phase	-0.071	-3.14	97	**.0044**	-0.12	-0.027	0.023	
Dependent Variable	**Independent Variable**	**Coefficient Estimate**	**Robust F statistic**	**df**	**p-value (from robust F test)**	**2.5% CI**	**97.5% CI**	**SE**	**Test Used**
p(Perseverative Error)	Group	0.022	2.27	1,97	.32	-0.0066	0.051	0.015	Robust Linear Model
	Age	-0.0013	0.030	1,97	.86	-0.016	0.013	0.0074	
	IQ	-0.0005	0.54	1,97	.46	-0.0017	0.00080	-0.72	
	Gender	0.031	4.20	1,97	.11	0.0018	0.060	2.078	

Key- df: degrees of freedom; BH: Benjamini-Hochberg correction; CI: confidence interval; SE: regression standard error; p(Correct): proportion correct choices; RT: mean reaction time; p(Switching following SNF): proportion of switching in response to spurious (false) negative feedback; p(Staying following VPF): proportion of staying in response to veracious (true) positive feedback; p(Perseverative Error): proportion of perseverative errors (only during reversal phase).

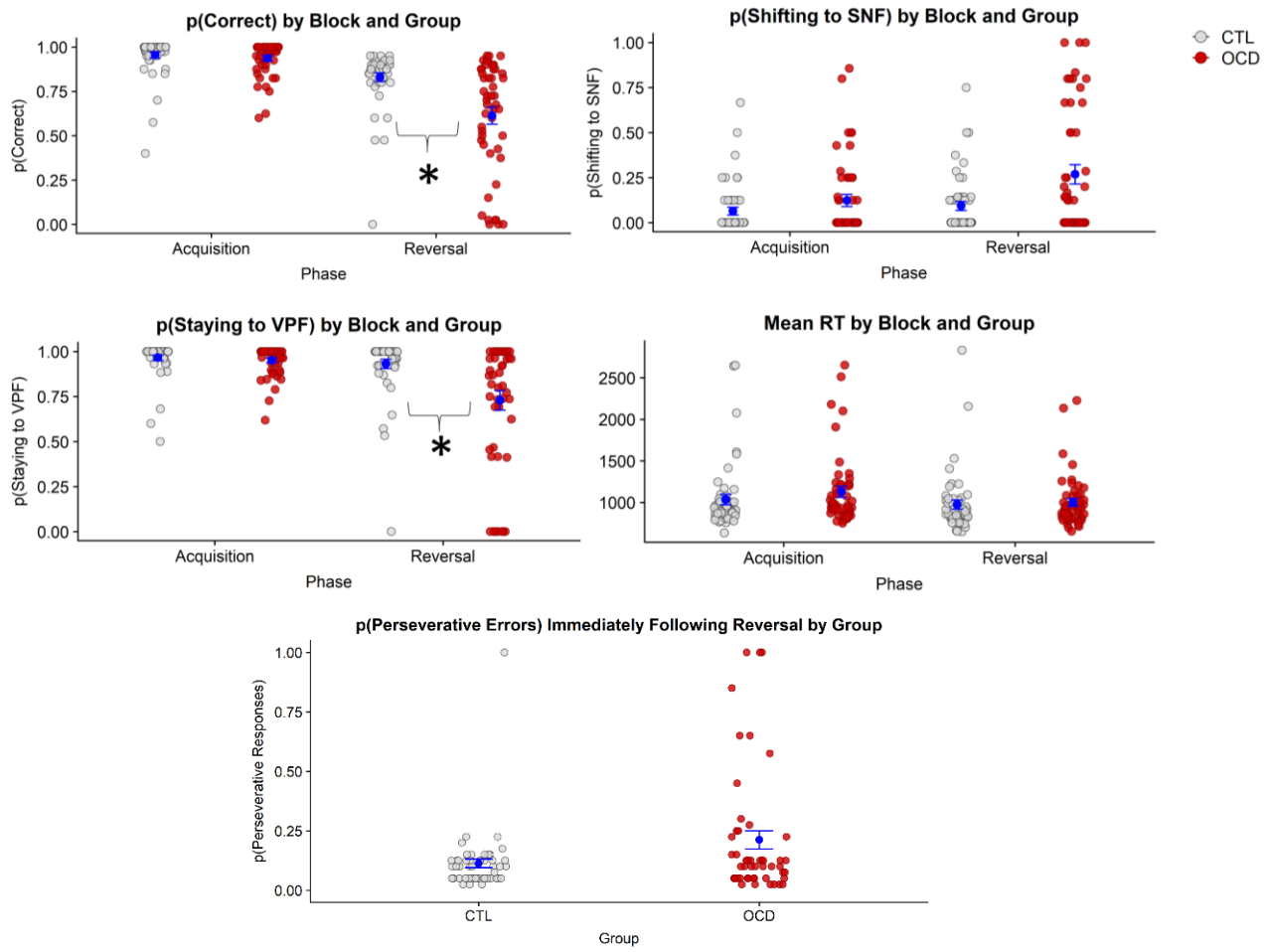

FIGURE 6.17: GROUP DIFFERENCE RESULTS ON MEASURES FROM PROBABILISTIC REVERSAL LEARNING TASK. OCD DISPLAYED LESS CORRECT RESULTS AND STAYED LESS FOLLOWING VERACIOUS POSITIVE FEEDBACK. NO SIGNIFICANT DIFFERENCES WERE FOUND ON OTHER MEASURES.

6.4.2 Standard Analyses of Effects of Medication

I proceeded to check for effects of medication status on participant behaviour on the probabilistic reversal learning task. Demographic, intelligence, and clinical scores per group after dividing OCD into MED+ and MED- are summarised in Table 6.4. No differences in gender, age, and IQ emerged between groups.

Table 6.4: Mean scores and standard deviations per group and statistical tests.

	CTL (n = 53)	MED- (n=20)	MED+ (n=30)	STATISTIC	PAIRWISE COMPARISONS
GENDER (F:M)	30:23	15:5	14:16	$\chi2$ (2)=3.96; *p*=.14	-
AGE	16.38 ± 2.05	16.34 ± 1.73	16.72 ± 1.79	$\chi2$ (2)=0.44; *p*= .80	-
WASI-II (IQ)[a]	109.11 ± 10.79	105.0 ± 11.85	107.57 ± 12.34	F(2,99) = .92; *p*= .40	-
BDI**	46.81 ± 6.43	56.30 ± 10.61	61.33 ± 10.55	$\chi2$ (2)=36.20; *p*= 1.38e-08	MED- & MED+ >CTL MED- = MED+
BAI**	48.04 ± 7.09	60.30 ± 12.38	64.50 ± 10.37	$\chi2$ (2)=42.74; *p*=5.24e-10	MED- & MED+ >CTL MED- = MED+
OCI**	9.25 ± 6.56	30.95 ± 14.08	27.97 ± 12.03	$\chi2$ (2)=57.31; *p*= 3.59e-13	MED- & MED+ >CTL MED- = MED+
CY-BOCS	NA	24.00 ± 5.13	23.13 ± 5.20	Z = 0.47, *p*=.64	-
Digit Span (Forwards) [b]	10.81 ± 2.79	12.00 ± 2.00	10.64 ± 2.66	F (2,37)=0.75; *p*=.48	-
Digit Span (Backwards) [b]	8.33 ± 2.15	7.63 ± 2.20	8.36 ± 1.63	F(2,37)=0.40; *p*=.67	-

Key: CTL: Control Group; MED-: Obsessive-Compulsive Disorder group; WISC-IV: Wecshler's Abbreviated Scale of Intelligence – II; IQ: Intelligence Quotient; BDI: Beck's Depression Inventory (t-scored); BAI: Beck's Anxiety Inventory (t-scored); OCI: Obsessive-Compulsive Inventory; CY-BOCS: Children's Yale-Brown Obsessive-Compulsive Scale. *p<.05; **p<.01, [a] missing data from one MED- participant; [b] data only available for 21 CTL, 8 MED-, and 11 MED+.

Post-hoc Dunn tests with Bonferroni correction revealed that MED+ and MED- had enhanced depression (MED- > CTL, p = .00099; MED+ > CTL, p = .000000033; MED+ = MED-, p = .63), anxiety (MED- > CTL, p = .00019; MED+ > CTL, p = .0000000021; MED+ = MED-, p = .68), and obsessive-compulsivity scores (MED- > CTL, p = .000000010; MED+ > CTL, p = .00000000064; MED+ = MED-, p = 1.00) compared to CTL. There were no differences in these ratings between MED+ and MED- (all p > .05).

Summary statistics and regression results for the task measures are summarised in Table 6.5 and 6.6 (also see Figure 6.4 for visualisation). MED- and MED+ were considered as separate variables compared to CTL in the regression models. For proportion correct, there were significant MED- -by-Phase (Coefficient Estimate = -0.17, t(100) = -4.56, p = .00006) and MED+-by-Phase (Coefficient Estimate =-0.093 , t(100) = -2.90, p = .018) interactions. Next, there was a significant interaction between MED- and Phase when considering proportion of stays following VPF (Coefficient Estimate =-0.12, t(100) = -4.11, p = .00017).

Table 6.5: Summary statistics (Mean ± Standard Deviation) for PRL task measures during acquisition and reversal phases.

	ACQUISITION			REVERSAL		
Dependent Variable	CTL	MED-	MED+	CTL	MED-	MED+
p(perseverative error)	-	-	-	0.11 ± 0.13	0.24 ± 0.29	0.19 ± 0.25
RT	1035.92 ± 401.98	1148.08 ± 511.15	1117.02 ± 373.29	975.41± 355.06	1005.78 ± 353.64	997.55 ± 281.18
p(Correct)	0.96 ± 0.11	0.93 ± 0.10	0.94 ± 0.097	0.83 ± 0.16	0.60 ± 0.29	0.63 ± 0.33
p(Switching following SNF)	0.064 ± 0.14	0.11 ± 0.21	0.13 ± 0.22	0.094 ± 0.16	0.27 ± 0.36	0.27 ± 0.34
p(Staying following VPF)	0.97 ± 0.098	0.95 ± 0.061	0.95 ± 0.093	0.93 ± 0.166	0.74 ± 0.31	0.73 ± 0.37

Key- CTL: control group; MED-: unmedicated patient group; MED+: medicated patient group; p(Correct): proportion correct choices; RT: mean reaction time; p(Switching following SNF): proportion of switching in response to spurious (false) negative feedback; p(Staying following VPF): proportion of staying in response to veracious (true) positive feedback; p(Perseverative Error): proportion of perseverative errors (only during reversal phase).

Table 6.6: Summary statistics and results from mixed linear regressions and robust mixed regressions. Mean and standard deviations per group (CTL, MED-, MED+) and per phase (Acquisition, Reversal) are reported. Wald's 95% confidence intervals were calculated. p(perseverative errors) has a separate section as different tests (robust linear regression and robust F-test) were used to analyse this measure. Significant variables and corresponding p-values are in bold.

Dependent Variable	Independent Variable	Estimate	Statistic (t)	df	BH-adjusted p-value	2.5% CI	97.5% CI	SE	Test used
p(Correct)	MED-	-0.027	-1.04	100	.38	-0.078	0.024	0.026	Robust Mixed
	MED+	-0.021	-0.90	100	.44	-0.065	0.024	0.023	Model
	Phase	-0.11	-5.83	100	**.000000268**	-0.15	-0.075	0.019	
	MED- x Phase	-0.17	-4.56	100	**.00006**	-0.24	-0.096	0.037	
	MED+ x Phase	-0.093	-2.90	100	**.018**	-0.16	-0.030	0.032	
RT	MED-	112.16	1.13	117.55	.38	-81.13	305.45	99.29	Mixed Linear
	MED+	81.10	0.94	117.55	.44	-87.19	249.38	86.45	Model
	Phase	-60.52	-2.04	100	.088	-118.28	-2.756	29.63	
	MED- x Phase	-81.79	-1.45	100	.20	-192.14	28.57	56.61	
	MED+ x Phase	-58.96	-1.20	100	.31	-155.04	37.12	49.29	
p(Switching following SNF)	MED-	0.030	0.80	100	.43	-0.043	0.10	0.037	Robust Mixed
	MED+	0.036	1.11	100	.44	-0.027	0.099	0.032	Model
	Phase	0.024	0.86	100	.39	-0.030	0.077	0.027	
	MED- x Phase	0.026	0.49	100	1.0	-0.077	0.13	0.052	
	MED+ x Phase	0.044	0.98	100	.33	-0.045	0.13	0.045	
p(Staying following VPF)	MED-	-0.025	-1.22	100	.38	-0.065	0.015	0.021	Robust Mixed
	MED+	-0.019	-1.05	100	.44	-0.054	0.016	0.018	Model
	Phase	-0.016	-1.08	100	.37	-0.046	0.013	0.015	
	MED- x Phase	-0.12	-4.11	100	**.00017**	-0.18	-0.062	0.029	
	MED+ x Phase	-0.045	-1.80	100	.15	-0.095	0.0041	0.025	

Dependent Variable	Independent Variable	Coefficient Estimate	Robust F statistic	df	p (from robust F test)	2.5%	97.5%	SE	Test Used
p(Perseverative Errors)	MED-	0.035	3.15	1,100	.38	-0.0023	0.073	0.019	Robust Linear
	MED+	0.013	0.61	1,100	.44	-0.020	0.046	0.017	Model

Key- MED-: unmedicated patient group; MED+: medicated patient group; M: mean; SD: standard deviation; df: degrees of freedom; BH: Benjamini-Hochberg Correction; CI: confidence interval; SE: regression standard error; p(Correct): proportion correct choices; RT: mean reaction time; p(Switching following SNF): proportion of switching in response to spurious (false) negative feedback; p(Staying following VPF): proportion of staying in response to veracious (true) positive feedback; p(Perseverative Error): proportion of perseverative errors (only during reversal phase).

The analyses were repeated controlling for age, gender, and IQ. The results still indicated significant MED--by-Phase (Coefficient Estimate = -0.15, $t(96) = -3.56$, $p = .0015$) and MED+-by-Phase (Coefficient Estimate = -0.13, $t(96) = -3.63$, $p = .0014$) interactions for proportion of correct responses. However, there was now a significant MED+-by-Phase interaction (Coefficient Estimate = -0.058, $t(96) = -2.29$, $p = .0048$), as well as a significant MED--by-Phase interaction (Coefficient Estimate = -0.096, $t(96) = -3.23$, $p = .0034$) for proportion of stays following VPF.

Table 6.6: Summary statistics and results from mixed linear regressions and robust mixed regressions (separating OCD into MED- and MED+). Age, gender, and IQ were controlled for. Wald's 95% confidence intervals were calculated. p(perseverative errors) has a separate section as different tests (robust linear regression and robust F-test) were used to analyse this measure. Significant variables and corresponding p-values are in bold.

Dependent Variable	Independent Variable	Estimate	Statistic (t)	df	p	2.5% CI	97.5% CI	SE	Test used
Correct	Age	0.0097	1.25	96	.53	-0.0055	0.025	0.0078	Robust Mixed Model
	Gender	-0.034	-2.12	96	**.018**	-0.065	-0.0025	0.016	
	IQ	0.0023	3.47	96	**.0032**	0.0010	0.0037	0.00067	
	MED-	-0.026	-0.90	96	.47	-0.084	0.031	0.029	
	MED+	-0.018	-0.74	96	.44	-0.067	0.030	0.025	
	Phase	-0.12	-5.58	96	**.00000032**	-0.16	-0.076	0.021	
	MED- x Phase	-0.15	-3.65	96	**.0015**	-0.23	-0.069	0.041	
	MED+ x Phase	-0.13	-3.63	96	**.0014**	-0.20	-0.059	0.035	
RT	Age	13.88	0.38	96	.89	-56.88	84.64	36.86	Mixed Linear Model
	Gender	34.43	0.46	96	.65	-110.48	179.35	75.50	
	IQ	-5.26	-1.64	96	.13	-11.41	0.90	3.21	
	MED-	105.83	1.03	112.068	.47	-92.37	304.03	103.27	
	MED+	67.04	0.76	112.265	.44	-101.35	235.43	87.74	
	Phase	-60.52	-2.05	99	.086	-118.14	-2.90	29.56	
	MED- x Phase	-95.22	-1.66	99	.13	-207.39	16.95	57.55	
	MED+ x Phase	-58.96	-1.20	99	.30	-154.80	36.89	49.17	
p(Switching following SNF)	Age	-0.015	-1.50	96	**.53**	-0.034	0.0045	0.0097	Robust Mixed Model
	Gender	-0.020	-1.00	96	.40	-0.059	0.019	0.020	
	IQ	-0.0022	-2.65	96	**.016**	-0.0039	-0.00059	0.00085	
	MED-	0.017	0.47	96	.47	-0.055	0.089	0.037	
	MED+	0.038	1.22	96	.44	-0.023	0.099	0.031	
	Phase	0.024	0.92	96	.36	-0.027	0.076	0.026	
	MED- x Phase	0.010	0.20	96	.84	-0.090	0.11	0.051	
	MED+ x Phase	0.046	1.04	96	.30	-0.040	0.13	0.044	
p(Staying following VPF)	Age	0.0050	0.89	96	.63	-0.006045	0.016	0.0056	Robust Mixed Model
	Gender	-0.022	-1.87	96	.11	-0.044	0.0011	0.012	
	IQ	0.0015	3.12	96	**.0060**	0.00057	0.0025	0.00049	
	MED-	-0.023	-1.10	96	.47	-0.065	0.018	0.021	
	MED+	-0.0143	-0.79	96	.44	-0.050	0.021	0.018	
	Phase	-0.017	-1.10	96	.36	-0.047	0.013	0.015	
	MED- x Phase	-0.096	-3.23	96	**.0034**	-0.15	-0.037	0.030	
	MED+ x Phase	-0.058	-2.29	96	**.0048**	-0.11	-0.0083	0.025	
Dependent Variable	**Independent Variable**	**Coefficient Estimate**	**Robust F statistic**	**Df**	**p (from robust F test)**	**2.5%**	**97.5%**	**SE**	**Test Used**
p(Perseverative Errors)	MED-	0.039	3.47	1,96	.47	-0.00016	0.0780	0.020	Robust Linear Model
	MED+	0.011	0.39	1,96	.44	-0.023	0.044	0.017	
	Age	0.0004	0.0027	1,96	.96	-0.014	0.015	0.0074	
	IQ	-0.0004	0.47	1,96	.49	-0.00170	0.00083	0.0006	
	Gender	0.032	4.48	1,96	.093	0.00260	0.062	0.015	

Key- MED-: unmedicated patient group; MED+: medicated patient group; M: mean; SD: standard deviation; df: degrees of freedom; BH: Benjamini-Hochberg Correction; CI: confidence interval; SE: regression standard error; p(Correct): proportion correct choices; RT: mean reaction time; p(Switching following SNF): proportion of switching in response to spurious (false) negative feedback; p(Staying following VPF): proportion of staying in response to veracious (true) positive feedback; p(Perseverative Error): proportion of perseverative errors (only during reversal phase).

As a result of the significant interactions, further post-hoc Wilcoxon tests with Bonferroni correction were conducted to make pairwise comparisons between CTL, MED-, and MED+. These analyses revealed that during the reversal phase, MED- and MED+ made less correct responses than CTL (MED- < CTL: Z = 3.61, p = .00031, Wilcoxon's r = 0.46; MED+ < CTL: Z = 3.61, p = .00030, Wilcoxon's r = 0.29; MED- = MED+: p = 1.00). Furthermore, MED- and MED+ stayed less following VPF compared to CTL (MED- < CTL: Z = 3.29, p = .00099; Wilcoxon's r = 0.42; MED+ < CTL: Z = 2.58, p = .01, Wilcoxon's r = 0.32; MED- = MED+: p =1.00).

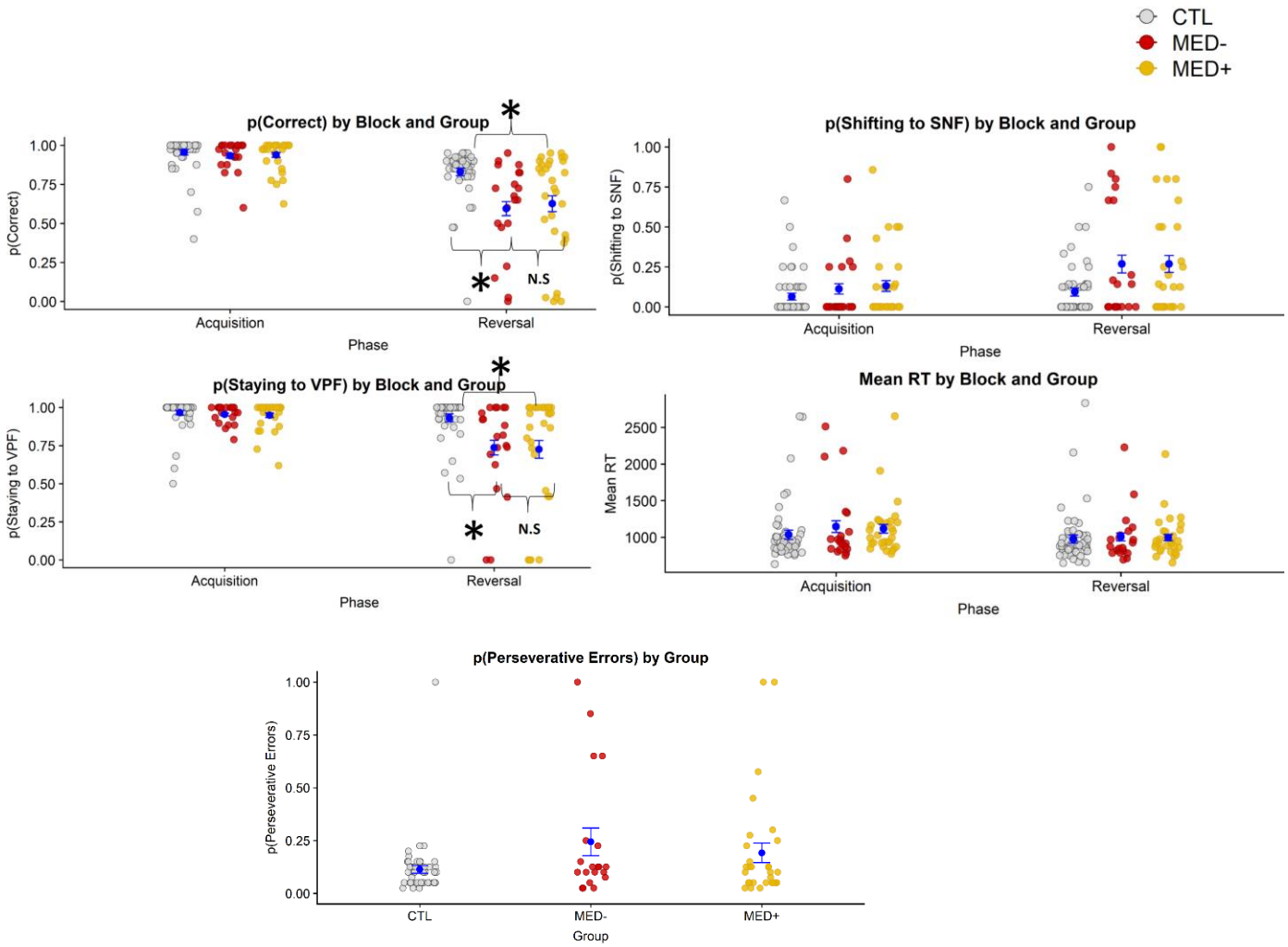

FIGURE 6.18: EFFECTS OF MEDICATION STATUS ON BEHAVIOUR ON THE PROBABILISTIC REVERSAL LEARNING TASK. MED- AND MED+ COMMITTED MORE ERRORS AND STAYED LESS FOLLOWING VPF DURING THE REVERSAL PHASE. NO SIGNIFICANT DIFFERENCES BETWEEN GROUPS EMERGED ON OTHER MEASURES. N.S.: NON-SIGNIFICANT

6.4.3 Computational Modelling Results

The winning model included the following parameters, reward rates, punishment rate, reinforcement sensitivity, and stimulus stickiness. A summary of the performances of each model is included in Table 6.7.

Table 6.7: Comparison of model performance

Rank	Model	Parameters	Log Marginal Likelihood	Log Posterior P (model)
4	1	α_{reinf}, τ_{reinf}	-1966.29	-42.92
2	2	α_{rew}, α_{pun}, τ_{reinf}	-1925.94	-2.57
1	3	α_{rew}, α_{pun}, τ_{reinf}, τ_{stim}	-1923.45	-0.080
3	4	α_{reinf}, τ_{reinf}, τ_{stim}	-1955.42	-32.05
5	5	ρ, φ, β	-1975.44	-52.07

Notes: The log marginal likelihood and log posterior P (model) are comparison metrics used to determine the best model. A numerically larger, i.e. less negative, log marginal likelihood is better. Model 3 was the best performing model here. Key – α: learning rate; rew: reward; pun: punishment; τstim: stimulus stickiness; τreinf: reinforcement rate (inverse temperature); ρ: rho; φ: phi; β: beta (inverse temperature).

Strikingly, OCD differed from CTL on all parameters considered. OCD displayed increased reward rates, lower punishment rates, lower punishment sensitivity, and lower stimulus stickiness (see Figure 6.5).

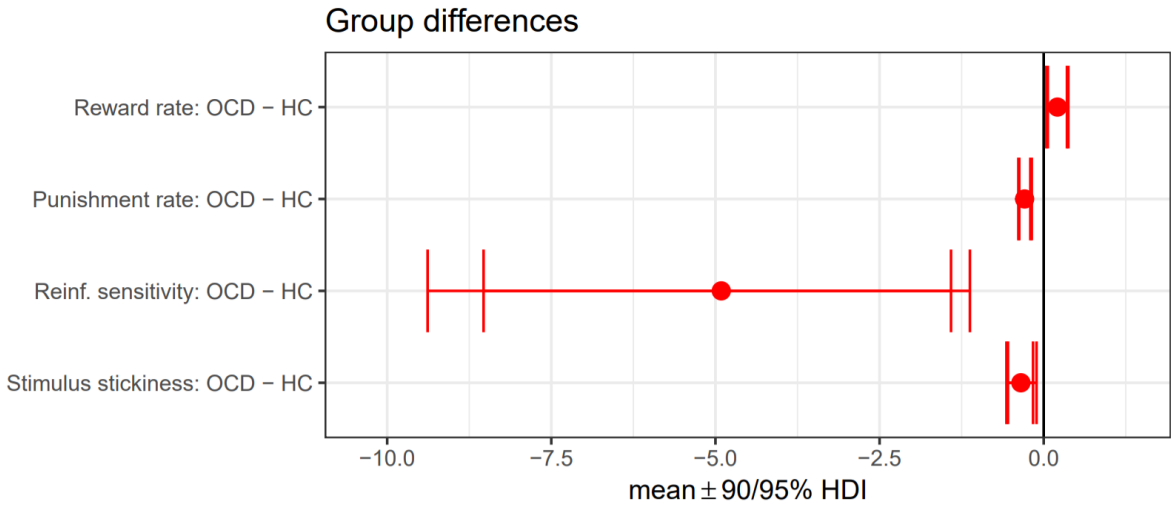

FIGURE 6.19: SUMMARY OF GROUP DIFFERENCES PER PARAMETER FROM THE BEST-FIT COMPUTATIONAL MODEL. ERROR BARS REPRESENT THE HIGHEST DENSITY INTERVALS (HDI) OF THE POSTERIOR DISTRIBUTIONS OF GROUP DIFFERENCES (OCD-CTL) IN GROUP MEAN PARAMETER VALUES. "RED" INDICATES THAT THE 95% HDI EXCLUDES 0 THUS INDICATING GROUPS DIFFER FROM EACH OTHER.

After dividing participants by medication status (CTL, MED-, and MED+), the same winning model was fit to data. It was found that MED- and MED+ differed from CTL on all parameters (see Figure 6.6). Similar to the CTL vs. OCD group analysis, both medication groups displayed increased reward rates, as well as decreased punishment rates, reinforcement sensitivity, and stimulus stickiness compared to CTL. There were no notable differences between MED- and MED+ across all parameters.

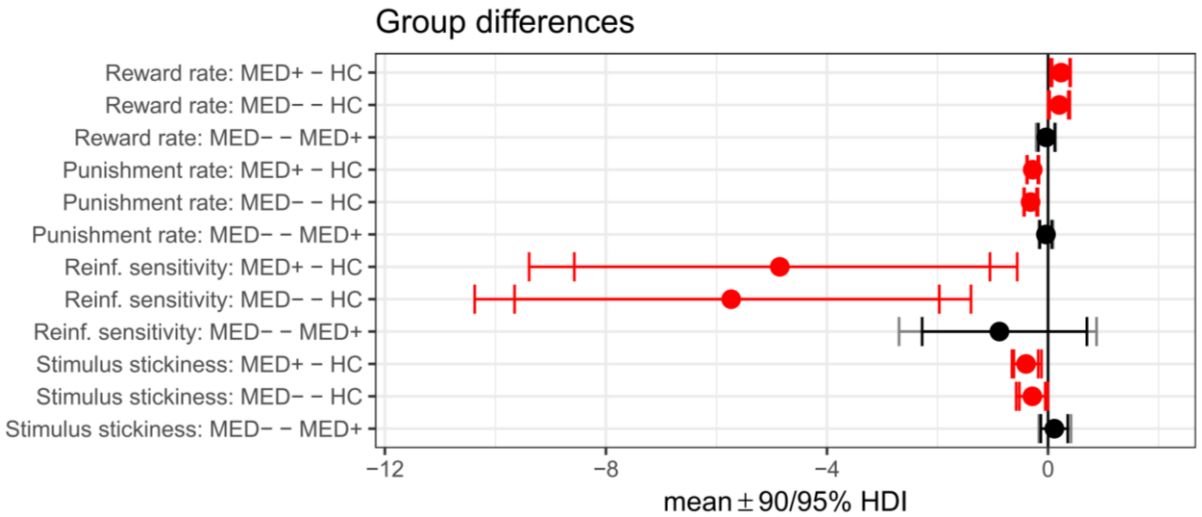

FIGURE 20.6: SUMMARY OF GROUP DIFFERENCES (PATIENTS WERE GROUPED ACCORDING TO MEDICATION STATUS) PER PARAMETER FROM THE BEST-FIT COMPUTATIONAL MODEL. ERROR BARS REPRESENT THE HIGHEST DENSITY INTERVALS (HDI) OF THE POSTERIOR DISTRIBUTIONS OF GROUP DIFFERENCES (OCD-CTL) IN GROUP MEAN PARAMETER VALUES. "RED" INDICATES THAT THE 95% HDI EXCLUDES 0 THUS INDICATING GROUPS DIFFER FROM EACH OTHER.

Parameter Recovery

Previously-fitted parameters used to generate the simulated data and their corresponding recovered values are presented in Table 6.8 for OCD vs CTL. All generative parameter values fell strictly within their corresponding recovered 95% highest posterior density intervals (HDI) and all 8 randomly initialised sampling chains were well-mixed, as indicated by the convergence diagnostic $\hat{R} \approx 1$ for every model parameter.

Table 6.8: Parameter recovery analysis with simulated data generated by best-fit computational model (CTL vs OCD)

Group	Parameter	Empirical Best-Fit	Simulated values	95% HDI Interval	R^
CTL	Reward Rate	0.28	0.31	[0.27, 0.36]	1.001
	Punishment Rate	0.58	0.59	[0.56, 0.62]	1
	Reinforcement Sensitivity	10.11	9.34	[8.47, 10.27]	1.001
	Stimulus Stickiness	0.41	0.44	[0.33,0.55]	1.002
OCD	Reward Rate	0.49	0.50	[0.45, 0.54]	1.001
	Punishment Rate	0.29	0.28	[0.25, 0.31]	1
	Reinforcement Sensitivity	5.20	5.24	[4.93, 5.56]	1.002
	Stimulus Stickiness	0.063	0.057	[-0.046, 0.16]	1.001

Key- CTL: control group, OCD: patient group, HDI: Highest density interval.

6.4.4 Correlations

Correlations between OCD/anxiety/depression severity and task/model measures

When considering all participants, those with higher anxiety scores (BAI) and obsessive-compulsive severity (OCI) made less correct responses on the task (BAI: r = -0.25, p = .010; OCI: r = -0.23, p = .017). Within CTL, higher anxiety scores were associated with less shifting following SNF (r =0.30, p = .042). Within MED+, higher OCI scores were associated with more stimulus stickiness (r =0.37, p =.047). There were no correlations between clinical questionnaires and task/model measures when considering only OCD or only MED-.

Correlations between age/IQ/working memory and task/model measures

When considering all participants, those with higher IQ and working memory (digit span backwards) scores made more correct responses (IQ: r = 0.27, p = .0052, digit span backwards: r = 0.33, p = .037), and shifted less following SNF (IQ: r = -0.27, p = .042, digit span backwards: r = -0.49, p = .0023). Better working memory was also associated with more stays following VPF (r = 0.47, p = .0021). When exploring relationships between demographic/clinical scores and model parameter values, I found higher IQ scores predicted increased punishment rate (r=0.21 p=.038), reinforcement sensitivity (r= 0.26, p= .008), and stimulus stickiness (r=0.24, p=.017). Additionally, age was correlated with reward rate, wherein older participants had increased reward rate values (r = 0.24; p = .016).

Next, when considering only OCD participants, IQ was found to be significantly correlated with punishment rate (r =0.33, p =.020), stimulus stickiness (r =0.32, p = .025), and proportion of correct responses (r =0.37, p =.0097).

Within CTL, better working memory was associated with less shifting following SNF (r =-0.61, p =.0032), more staying to VPF (r =0.59, p =.0046), more correct responses (r =0.62, p =.0025), and faster reaction times (r= -0.52, p = .016). Older participants had increased reward rates (r =0.30, p =.032), less shifting following SNF (r =-0.28, p =.035), more staying following VPF (r =0.28, p =.041), and increased correct responses (r =0.34, p =.013).

Within MED-, older participants had higher reward rates (r =0.51, p =.021).

No significant correlations between age/IQ/working memory and task/model measures were detected when considering only MED+.

Correlations with medication dosage

Medication dosage significantly correlated with IQ scores (r = 0.43; p = .017). Dosage did not show any significant relationships with task measures or model parameter values.

Correlations between standard task measures and computational model parameters

Lastly, to verify that, and understand how, model parameter values map onto task behaviour, further Pearson correlations between model parameter values (reward rate, punishment rate, reinforcement sensitivity, and stimulus stickiness) and standard task measures (proportion correct, proportion shifting following SNF, proportion staying following VPF, proportion perseverative errors, and mean response times) were conducted. These analyses were conducted first considering all participants,

then considering OCD, CTL, MED-, and MED+ separately. The results of this are included in Table 6.9.

Table 6.9: Correlations between standard task measures and model parameters for all participants, OCD only, CTL only, MED- only, and MED+ only.

All Participants	p(Correct)	p(Switch following SNF)	p(Stay following VPF)	p(Perseveration)	Mean RT
Reward rate	r = 0.22	n.s	*r* = 0.41	n.s	n.s
	p = .029		*p* <.0001		
Punishment rate	*r* = 0.66	n.s	*r* =0.29	*r* = -0.48	n.s
	p <.0001		*p* =.0034	p <.0001	
Reinf. Sensitivity	*r* = 0.36	*r* = -0.75	*r* = 0.83	*r* = 0.31	*r* =-0.30
	p = .00020	*p* <.0001	*p* <.0001	*p* = .0015	*p* =.0020
Stim. Stickiness	n.s	*r* = -0.56	*r* = 0.40	n.s	*r* = -0.21
		p <.0001	*p* < .0001		*p* = .030
OCD only	p(Correct)	p(Switch following SNF)	p(Stay following VPF)	p(Perseveration)	Mean RT
Reward rate	n.s	n.s	n.s	n.s	n.s
Punishment rate	r = 0.81	n.s	r = 0.37	r = -0.45	n.s
	p <.0001		*p* = .0073	*p* = .00096	
Reinf. Sensitivity	r =0.31	r = -0.82	r = 0.88	r = 0.377	r = -0.37
	p = .031	*p* <.0001	*p* < .0001	*p* = .0070	*p* = .0088
Stim. Stickiness	n.s	r = -0.59	r = 0.52	n.s	r = -0.38
		p <.0001	*p* = .00010		*p* = .0059
CTL only	p(Correct)	p(Switch following SNF)	p(Stay following VPF)	p(Perseveration)	Mean RT
Reward rate	*r* = 0.58	*r* = -0.68	*r* = 0.83	n.s	n.s
	p<.0001	*p*<.0001	*p* <.0001		
Punishment rate	r = 0.50	n.s	n.s	*r* = -0.66	n.s
	p = .00014			*p* < .0001	

Reinf. Sensitivity	r = 0.56 *p* <.0001	*r* = -0.73 *p* < .0001	*r* = 0.79 *p* <.0001	n.s	n.s
Stim. Stickiness	n.s	*r* = -0.57 *p* < .0001	n.s	n.s	n.s
MED- only	p(Correct)	p(Switch following SNF)	p(Stay following VPF)	p(Perseveration)	Mean RT
Reward rate	n.s.	n.s.	n.s.	n.s.	n.s.
Punishment rate	r = 0.66 *p* = .00015	n.s.	n.s.	n.s.	n.s.
Reinf. Sensitivity	n.s.	r = -0.74 *p* = .00021	r = 0.90 *p* < .0001	r = 0.49 *p* = .030	r = -0.50 *p* = .024
Stim. Stickiness	n.s.	n.s.	n.s.	n.s.	r = -0.59 *p* = .0065
MED+ only	p(Correct)	p(Switch following SNF)	p(Stay following VPF)	p(Perseveration)	Mean RT
Reward rate	n.s	n.s.	n.s.	n.s.	n.s.
Punishment rate	r = 0.88 *p* < .0001	n.s.	r = 0.41 *p* = .023	r = -0.49 *p* = .0060	n.s.
Reinf. Sensitivity	r = 0.37 *p* = .042	r = -0.72 *p* < .0001	r = 0.88 *p* < .0001	n.s.	n.s.
Stim. Stickiness	n.s.	r = -0.72 *p* < .0001	r = 0.59 *p* = .00057	n.s.	n.s.

Key: r – Pearson's r statistic, p – significance value; n.s – not significant; OCD – patient group; CTL – control group

6.4.5 Summary of Main Results

When conducting standard behavioural analysis, OCD were found to display less correct responses and less staying to VPF during the reversal phase compared to CTL. The same pattern of results was observed when splitting OCD into MED- and MED+; both patient groups showed less correct

responses and less staying following VPF after reversal compared to CTL, but there were no significant differences when comparing MED- and MED+ to each other. Group differences remained significant even when controlling for age, gender, and IQ.

Modelling analyses indicated that compared to CTL, OCD (as well as MED+ and MED-) had increased reward learning rate parameters, and decreased punishment learning rate, reinforcement sensitivity, and stimulus stickiness parameters.

6.5 Discussion

This study aimed to disentangle the cognitive processes contributing to behaviour on a well-known probabilistic reversal learning paradigm in adolescents with OCD. Standard analysis of task behaviour revealed a reversal deficit in adolescents with OCD, wherein patients made significantly more incorrect responses and repeated choices less following veridical positive feedback. Nonetheless, patients and controls showed equivalent acquisition learning of the task. Next, I fit a Bayesian hierarchical reinforcement learning model to data and results indicated substantial distinctions in the performance profiles of patients and controls. Adolescents with OCD displayed increased reward learning rates and heightened choice exploration, alongside lower punishment learning rates and lower stimulus stickiness (perseveration) compared to healthy adolescents.

6.5.1 Standard behavioural findings

My standard behavioural results indicate intact probabilistic learning but impaired reversal learning in adolescents with OCD. Impaired performance following reversal implies a behavioural flexibility deficit in adolescent patients, where they are not able to update their decisions as efficiently as healthy adolescents when there are changes in contingencies. The majority of previous work probing cognitive flexibility in children with OCD (see Chapters 1 and 2) has failed to detect a flexibility deficit, likely due to studies administering tasks with deterministic pay-offs such as the Intra-Extra Dimensional Shift task and Wisconsin Card Sorting Task. My standard results suggest that behavioural flexibility is heavily compromised in adolescents with OCD on tasks with probabilistic structures.

Next, when assessing behaviour in response to feedback, I found that adolescent patients showed a significant tendency to shift away from responding to the optimal stimulus after receiving positive feedback. This is consistent with previous work by Hauser et al. (2017) who reported a trend for their OCD sample (which included 22 adolescents and 10 adults) to switch choices more frequently following rewards on a probabilistic reversal learning task. Moreover, Apergis-Schoute et al. (in-prep) found that adults with OCD were more likely to switch away from the optimal stimulus

following both negative and positive feedback on the exact same version of the task I have administered. One explanation for this increased shifting behaviour regardless of feedback is that it indicates an overall tendency for adults and adolescents with OCD to keep returning to the stimulus that was once optimal. This could be a form of perseveration/inflexibility whereby responding to the previously optimal stimulus is now ingrained behaviour and interferes with patients' ability to re-learn the appropriate contingencies in the reversal phase, and may be analogous to unwanted intrusions experienced by patients in daily life.

6.5.2 Modelling Results

Intriguingly, modelling results suggest an alternative portrayal of behaviour on the task, as adolescents with OCD actually showed increased reward learning rates and lower punishment learning rates despite standard analyses showing increased shifting from veridical positive feedback. Moreover, instead of being more perseverative, modelling revealed that adolescents with OCD made more exploratory choices and had lower stimulus stickiness. Hence, it is now necessary to explain this apparently discrepant and paradoxical set of conclusions obtained from the two means of analysing the data, i.e. via conventional and computational methods.

Learning rates in the model quantify how quickly one learns from most recent feedback compared to information accumulated over time. In the current task, the learning rates were used to estimate the extent to which values associated with a choice changed according to immediate positive and negative feedback, in other words, the extent to which positive and negative feedback respectively increased and decreased the value of a choice. Alongside the learning rates, the reinforcement sensitivity parameter represented whether participants' actual decisions reflected the values assigned to each choice. Concretely, a participant with a high reinforcement sensitivity parameter would more likely maximise their rewards by always choosing the choice perceived to have a higher value. In contrast, a participant with a low reinforcement sensitivity parameter would make more inconsistent decisions which are not in accordance with choice values.

Increased reward learning rates and lower punishment learning rates in adolescents with OCD indicate they are likely to update choice values more rapidly following recent positive feedback, compared to negative feedback. Despite higher reward rates compared with controls, patients do not seem to be using these updated values to guide their choices, as evident from their low reinforcement sensitivity values. Further evidence for this can be found in the correlational results, where reward learning rates correlate strongly with staying to veridical positive feedback in healthy adolescents but not in patients. Hence, healthy adolescents with higher reward rates expressed more staying

behaviour following positive feedback while the same increased reward rates did not translate to more reward-driven behaviour on the task in adolescents with OCD. Instead, in the OCD group, appropriate staying to optimal choices and proportion correct responses correlated with the punishment rate and reinforcement sensitivity parameter values. This suggests that incorrect responses and maladaptive switching to rewards displayed by patients are better explained by reduced punishment learning rates and a propensity for choice exploration compared to heightened reward rates.

Next, in contrast to the interpretation put forward for the standard behavioural results, decreased stickiness (reflecting the tendency for a choice to be repeated from trial to trial) and higher exploration in OCD from the modelling results suggest that adolescent patients are not perseverative on this task, and that their tendency to keep returning to the previously optimal stimulus in the reversal phase is the result of lower value-driven responding and not a form of perseveration as was previously considered.

Trial-by-trial modelling results and their relationships to standard task measures enable richer interpretation of and detailed insight into behavioural performance. Other computational papers have also highlighted differences in results obtained from modelling and standard analyses, for instance Apergis-Schoute et al. (in-prep) found increased shifting from punishment and rewards in their adult OCD population but reported no differences in model learning rates between patients and controls. Moreover, other studies found no behavioural deficits associated with OCD when employing standard analyses but uncovered decreased stimulus stickiness in patients when conducting computational modelling (Hauser et al., 2017; Kanen et al., 2019). Including my current study, all studies that have conducted computational modelling of probabilistic reversal learning data have found that OCD patients show decreased stimulus stickiness, or decreased stimulus stickiness and increased exploration, despite different results garnered via standard analyses. This challenges findings from past papers that have employed the probabilistic reversal learning task to patients with OCD (Chamberlain et al., 2008; Endrass et al., 2011; Tezcan, Tumkaya, & Bora, 2017; Viswanath et al., 2009) and the interpretations authors have made based solely on results from standard frequentist analyses.

6.5.3 Exploration and reduced stickiness

The next sections will discuss the implications of the modelling findings in the context of juvenile-OCD. First, increased exploration indicates that adolescents with OCD maximise their rewards less in favour of making more random choices, while reduced stickiness indicates a tendency to switch

more frequently between choices. The characteristics appear to be stable across the lifespan as they are also present in adult patients (Apergis-Schoute et al., in-prep; Hauser et al., 2017; Kanen et al., 2019), and may therefore be important features underpinning cognition in OCD. A few explanations for these findings are presented here but more in-depth analysis and discussion of exploration in OCD is available in Chapter 7 of this thesis.

How living things accumulate evidence and make decisions using exploratory or exploitative strategies has long been researched and debated. Literature discussing the explore-exploit dilemma establishes that some exploration can be advantageous to learning: while exploitation maximises rewards in the near-term, information obtained during exploration (by sampling novel choices) can be used to maximise rewards in the long-term (Barack and Gold, 2016). Moreover, in a dynamic environment, where values of all potential options are uncertain, it is considered conducive for an individual to be able to adapt their behaviour by flexibly alternating between exploratory and exploitative strategies (Addicott, Pearson, Sweitzer, Barack, & Platt, 2017). In addition, empirical research has highlighted the existence of different forms of exploration. First, *directed exploration* involves weighing known choice values and choosing a novel option to improve pre-existing knowledge of all options present in an environment. Inversely, *random exploration* is not based on known values and is equivalent to flipping a coin to decide on an option to choose. It has been found that healthy adults engage in both forms of exploration to maximise their long term rewards (Gershman, 2018; Wilson, Geana, White, Ludvig, & Cohen, 2014).

In the current study, exploration displayed by adolescents with OCD does not appear to be directed, or for the purpose of long-term maximisation, as their performance on the task is inferior to that of healthy adolescents who explore less. Hence, perhaps adolescents with OCD are engaging in random exploration which does not take into account values associated with competing choices. As a result of being value-independent, random exploration is a far less cognitively demanding strategy than directed exploration but it comes at the cost of suboptimal choices, and has been found to be conducted primarily by children and young adolescents whose frontal lobes and higher order thinking skills are still in the process of developing (Dubois et al., 2020). Some past studies offer support for poor goal-directed control and planning in children and adolescents with OCD (Gottwald et al., 2018; Huyser et al., 2010; Kim et al., 2018; Ornstein et al., 2010), suggesting that it may have been easier for adolescents with OCD in my study to rely on the random exploration heuristic over engaging in more cognitively complex directed exploration. Nonetheless, this interpretation is speculative for now as the current probabilistic reversal task was not designed to investigate random vs. directed exploration.

Another explanation for increased exploration seen here is that adolescents with OCD switch choices more as they feel increased subjective uncertainty regarding choice values. Indeed, it has been found that patients with OCD report more subjective uncertainty than healthy people (Stern et al., 2013). Moreover, past studies demonstrate that increasing task uncertainty promotes more exploratory behaviour in healthy people (Parr & Friston, 2017; Stojic et al., 2020). More convincingly, increased information seeking behaviour or exploration has been detected in adults and children with OCD on tasks where uncertainty is enhanced or when pay-offs are probabilistic (Banca et al., 2015; Erhan et al., 2017; Hauser et al., 2017; Mandali, Weidacker, Kim, & Voon, 2019), but not in tasks with deterministic structures (Apergis-Schoute et al., in-prep, see Chamberlain et al., 2020 and Marzuki et al., 2020 for reviews). A computational model of OCD developed by Fradkin et al. (2020) posits that individuals with OCD are unable to predict how different actions result in specific outcomes depending on certain states, resulting in increased sensations of uncertainty. Patients seek to reduce this uncertainty by engaging in compulsions such as repeated checking. Relevant to the current task, Hauser et al. (2017) suggest decreased choice consistency displayed by adolescents with OCD may be analogous to checking behaviour, wherein patients frequently check the non-optimal stimulus to ensure it is delivering the predicted feedback.

Alternatively, instead of exploring, patients with OCD may be making less valuable decisions simply because they are not aware of values associated with each choice or are unable to distinguish between choices with high and low values. Evidence for this can be found in research administering perceptual decision-making tasks to patients and modelling the data using drift-diffusion models. These models have been described in depth in Chapter 4, but in brief they involve modelling response times to describe how subjects accumulate evidence and whether speed or accuracy is favoured in decision-making. Research into OCD utilising these models demonstrate that patients are impaired at evidence accumulation; they are slower to make decisions (suggesting increased evidence accumulation) but despite this, they have difficulty discriminating between different choice values (Banca et al., 2015; Erhan et al., 2015; Mandali et al., 2019). In other words, all choices presented appear equally rewarding to patients, resulting in more random responding and more mistakes. In addition, adult OCD patients, and even healthy adults with compulsive tendencies, have been found to be impaired at using accumulated evidence to drive decisions and instead rely on highly salient recent feedback (Vaghi et al., 2017; Seow et al., 2020). This indicates that the disorder impairs the ability to synthesise information learnt over time, making it more difficult to construct accurate representations of values associated with all possible decisions. Recently, computational studies have combined traditional reinforcement learning models with drift diffusion models to model data from

probabilistic learning tasks, as this amalgamated model offers rich insight into value-driven decision-making beyond just classing people as being either exploitative or exploratory (Fontanesi et al., 2019; Pedersen et al., 2017; Wiehler & Peters, 2020). I had also fitted a version of this model to data from a sequential decision-making task in Chapter 4. Future work into probabilistic reversal learning in OCD should utilise such models to truly understand whether value-less decision-making is due to exploration or poor representation of choice values.

What appears to be random exploration may also be the result of attentional lapses. Poor attention may be 1) impacting learning of values associated with choices or 2) resulting in patients not using learnt value-knowledge to make decisions. Attentional deficits are present in adult patients with OCD, as reported by a meta-analysis revealing attentional control in patients to be impaired in across several studies, with moderate effect sizes (Abramovitch et al., 2013). However, evidence is less consistent in child-OCD studies, as so far only two studies have detected attentional impairments in child patients (Baykal et al., 2014; Chang et al., 2007) while two other studies did not find deficits (Okazaki et al., 2018; M. S. Shin et al., 2008). Alternatively, difficulty learning choice values as well as keeping different choice values in memory may be causing random responding in adolescent patients, consistent with research suggesting learning and memory impairments are associated with juvenile-OCD (Gottwald et al., 2018).

There is also neural evidence for abnormal exploration associated with OCD that is alluded to in Chapter 4 and discussed in detail in Chapter 7.

All in all, there are various viable reasons introduced for reduced choice consistency in adolescents with OCD, namely a bias for random exploration due to reduced cognitive control, poor representation of choice values, as a means to reduce subjective uncertainty, and attentional or learning deficits. Future studies employing more sophisticated models of exploration and evidence accumulation, specific tasks designed to probe different types of exploration under different circumstances (e.g. manipulating task uncertainty), and neuroimaging methods are necessary to truly understand how and why exploration is aberrant in OCD.

6.5.4 Reward and Punishment Rates

Next, modelling results indicate that adolescents with OCD and healthy adolescents learn from feedback differently, with patients updating choice values more following rewarding feedback and controls updating choice values more following punishing feedback. This is a novel finding in the context of OCD as majority of pertinent studies do not find differences in learning rates between groups (Apergis-Schoute et al., in-prep; Hauser et al., 2017; Kanen et al., 2019). In contrast, there is

evidence to suggest that adults with OCD exhibit increased learning rates following negative prediction errors (Vaghi et al., 2017) and even evidence for adult patients to display reduced learning rates on a probabilistic learning task (Murray et al., 2018). However, these two studies did not utilise separate learning rates for reward and punishment in their respective models, and also did not employ probabilistic reversal learning paradigms, so it is difficult to draw parallels to my findings.

Also in contrast to my findings, some neural evidence highlights blunted reward processing but elevated punishment processing in adults with OCD: presentation of rewarding feedback during learning tasks was associated with reduced activation in frontal regions (medial OFC, medial and superior frontal cortex, and cingulate cortex) while presentation of punishment was associated with overactivation in the same regions in patients (Kaufmann et al., 2013; Remijnse et al., 2009). However, there is also evidence for enhanced reward processing in OCD, as one study has described increased activity in frontostriatal regions during reward anticipation in medication-naïve adult OCD patients (Jung et al., 2011). Within paediatric OCD, decreased activation associated with wins (putamen/caudate) and losses (medial prefrontal cortex) has been found in child patients compared to controls (Norman et al., 2018), suggesting young patients have overall dampened feedback processing. Accumulatively, these findings suggest that feedback processing as a whole is atypical in adult- and child-OCD regardless of feedback valence. My study did not employ neuroimaging methods so I am unable to extrapolate how reward and punishment rates are represented in the brain circuitry of the current adolescent patient sample, but this should be considered in future research.

Adolescents with OCD perhaps only appear more reward sensitive because they are compared to healthy adolescents who are especially affected by punishing feedback. Emerging research reveals that healthy younger people are significantly more punishment sensitive than healthy adults (Hauser et al., 2015; Rodriguez Buritica et al., 2019; Rosenbaum, Grassie, & Hartley, 2020; van den Bos et al., 2012). Indeed, in my current study, reward learning rates increased with age in the healthy control group confirming that reward seeking behaviour emerges with development. I propose that adolescents with OCD, in contrast to healthy adolescents, are not particularly sensitive to either kind of feedback given that they favour exploratory over value-driven decision-making and show attenuated frontostriatal activation to both positive and negative feedback (Norman et al., 2018). This account is compatible with the clinical presentation of OCD, where patients' worries and rituals are out of proportion with and unaffected by information available in the external environment.

6.5.5 Correlations

It is unclear in this study whether abnormal choice exploration and feedback sensitivity are driven by the symptoms of OCD or vice versa, as disease severity did not correlate with any model measures, in comparison to Apergis-Schoute et al.'s study in adults where OCD severity correlated with reduced stimulus stickiness. In addition, serotonergic medication does not seem to improve performance as medicated and unmedicated patients in this study showed similar patterns of behaviour on the task. This implies that abnormal performance on this task is a stable trait of OCD, unperturbed by treatment or severity of symptoms. Moreover, it may be a stable trait across the lifespan as impairments are expressed by both juvenile and adult patient populations.

It is also important to highlight that even though adolescents with OCD in this study had elevated anxiety and depression scores compared to healthy controls, these features do not appear to be driving abnormal performance as anxiety and depression did not correlate with any model parameter values. In addition, exploration and reduced perseveration displayed here by adolescents with OCD are generally different from behaviour displayed by populations with anxiety or depression (Brolsma et al., 2020; Lighthall, Gorlick, Schoeke, Frank, & Mather, 2013; Mather & Lighthall, 2012; Ting et al., 2020). Nonetheless, the possible roles of anxiety and depression on decision-making are discussed further in Chapter 7.

Instead, IQ and working memory scores were predictive of better task performance and less extreme model parameter values in both patients and controls, which has also been detected in previous chapters. Thus, higher order cognition may be a protective factor against impaired decision-making in adolescent-OCD, which has implications for the importance of education and cognitive training in ameliorating cognitive deficits associated with the disorder. Although, evidence for the benefits of cognitive training, particularly in the context of OCD, is quite limited (Buhlmann et al., 2006). This is also discussed in Chapter 7.

6.5.6 Conclusions

Using computational methods, I demonstrate that adolescent-OCD is associated with altered feedback sensitivity, reduced perseveration, and enhanced exploration leading to significantly impaired performance on a probabilistic reversal learning paradigm. These findings are mostly compatible with the adult literature, demonstrating that deficits in decision-making on this task are stable across the lifespan in OCD. However, findings related to reward and punishment rates are divergent from studies employing adult patients. Further research comparing adult- and adolescent-OCD subtypes, as well as longitudinal developmental research, are required to understand how

feedback sensitivity is altered in OCD and with age. Overall, the current findings align with recent theoretical accounts highlighting disadvantageous decision-making and maladaptive information seeking in OCD when environments are stochastic or volatile.

Chapter 7: General Discussion

The experimental chapters in this thesis sought to understand latent cognitive processes contributing to complex learning and decision-making in adolescents with OCD. Some chapters also attempted to establish whether cognitive mechanisms found to be reliably impaired in adults with OCD are similarly disrupted in juvenile-OCD, namely model-based reasoning, cognitive flexibility, meta-cognition, and punishment sensitivity. Overall, I aspired to further current knowledge of the neurocognitive profile of adolescent-OCD as well as gain insight into the cognitive differences between adult and adolescent OCD subtypes.

7.1 Summary of findings

Past studies assessing cognitive flexibility in youths with OCD have reported varied results. Consequently, I aimed to understand whether adolescents with OCD showed divergent latent decision-making processes from healthy adolescents on the well-known Wisconsin Card Sorting Task in Chapter 2. Overall I found no significant differences between patient and control groups on any task measures when controlling for age, gender, and IQ. Additionally, there were no group differences detected when conducting computational modelling analyses. Significant group differences only emerged when separating the OCD group by medication status (medicated vs unmedicated). Those medicated with SSRIs were found to make more unique errors on the task than other groups, indicating that they were more likely to select the deck that did not correspond with any rule on the test card. Medicated patients also showed overall increased response times compared to control participants. These findings were interpreted as medicated patients having less recognition of rules present in the task, potentially as a result of difficulties with attending to multiple rules at once. Moreover, increased response times were inferred to be due to patients being more uncertain about the rules and perhaps needing more time to reach a decision, consistent with research reporting more careful evidence accumulation in adolescents with OCD (Hauser et al., 2017). Nonetheless, despite the tendency for committing more unique errors, performance was overall unimpaired in both medicated and unmedicated patient groups. Crucially, those with OCD did not make more perseverative errors than controls did on the task, confirming that adolescents with OCD have intact cognitive flexibility which is divergent from findings in adult patients.

In Chapter 3, I probed instrumental and Pavlovian processing in adolescents with OCD using an aversive Pavlovian-to-Instrumental Transfer task. I hypothesised that adolescents with OCD would show poor performance on the Instrumental and Pavlovian learning phases of the task, in line with literature showing instrumental and implicit learning deficits in youths with OCD (Gottwald et al.,

2018; Vloet et al., 2010). Next, specific and general transfer during the PIT phase of the task are thought to correspond to model-based and model-free learning respectively (Dolan & Dayan, 2013), and I hypothesised that my patient group would show reduced specific transfer and intact general transfer, which corresponds to research showing poor model-based decision-making in adult OCD (Voon, Derbyshire, et al., 2015), and is consistent with altered OFC functioning in OCD (Chamberlain et al., 2008; Remijnse et al., 2006; 2009). Lastly, I predicted increased avoidance responding in the Instrumental and PIT phases by adolescents with OCD consistent with accounts of increased harm avoidance reported by children with OCD (Bey et al., 2017; Cervin et al., 2020; Ecker & Gönner, 2008; Ettelt et al., 2008). Contrary to these hypotheses, adolescents with OCD showed equivalent performance to healthy controls across all phases of the PIT task, indicating 1) intact Pavlovian and instrumental learning, 2) intact model-based ability to transfer top-down information garnered during instrumental and Pavlovian phases to conduct successful specific PIT, and 3) no evidence of excessive harm avoidance. I reason that the aversive context of the task may have motivated adolescents with OCD to correctly learn US-response and CS-US pairings and retain this information throughout the task, consistent with new research showing superior safety learning in people with compulsive and anxious traits (Wise & Dolan, 2020). The only differences found between groups in this chapter were that adolescents with OCD reported reduced confidence in their explicit CS-US associations during the Pavlovian phase. This finding was most prominent in patients medicated with SSRIs. I proposed that this was due to a meta-memory deficit in adolescents with OCD, which is often reported in adult OCD patients (Boschen & Vuksanovic, 2007; Hermans et al., 2008; MacDonald, Antony, MacLeod, & Richter, 1997; Tolin et al., 2001). However, findings from Chapter 5 (see below) challenge this meta-cognitive theory. I concluded that avoidance learning and Pavlovian-to-instrumental transfer are unimpaired in adolescents with OCD.

As chapters thus far which used deterministic tasks overall showed no major deficits in OCD, the last 3 experimental chapters employed probabilistic tasks, in line with emerging research revealing that OCD patients display disadvantageous decision-making when choice pay-offs are stochastic (Norman et al., 2018; Pushkarskaya et al., 2015). Following on from the last chapter that indirectly probed model-based/model-free behaviour, I formally investigated whether model-based reasoning was reduced in adolescent OCD using a equential decision-making task in Chapter 4. To derive holistic measures of model-based behaviour, I took into account choices and response times of participants when conducting standard statistical analysis. Moreover, I fitted a reinforcement learning drift diffusion model (RL-DDM, Shahar et al., 2019) to data to determine latent processes contributing to model-based reasoning as well as decision-making overall. Contrary to research in

adult OCD (Voon, Derbyshire, et al., 2015), adolescents with OCD did not significantly differ from healthy controls on any of the model-based measures investigated. I inferred that either impaired model-based reasoning only emerges in adulthood in individuals with OCD or that the disorder disrupts healthy maturation of model-based reasoning over time. Next, results from the RL-DDM revealed that patients made more exploratory (or less value-guided) decisions, as well as faster and less accurate decisions, during Stage 2 of the task. These findings were most prominent in medicated patients. Increased exploration seen here is congruent with past research showing reduced choice consistency in OCD patients on probabilistic tasks (Apergis-Schoute et al., in-prep; Norman et al., 2017), and is thought to be driven by higher subjective uncertainty leading to frequent checking of sub-optimal options. Past papers also report that OCD patients over-recruit brain regions including vmPFC and dACC important for exploratory strategies (Apergis-Schoute et al., 2017; Carrasco, Harbin, et al., 2013; Stern et al., 2013), suggesting heavy reliance on this heuristic and inability to switch between exploitative and exploratory strategies effectively. Favouring speed over accuracy was thought to be due to trials in this task terminating if subjects took too long to answer, consistent with a study showing OCD patients make faster responses and accumulate less evidence when penalised for slowness (Banca, Vestergaard, et al., 2015). Thus, I concluded that while model-based reasoning overall is normal in adolescents with OCD, their decision-making appears atypical from that displayed by healthy adolescents.

Influenced by research that revealed a novel confidence-action dissociation in adults with OCD (Vaghi, Luyckx, et al., 2017), I administered a predictive-inference task to adolescents with OCD to assess whether action and confidence are equally decoupled in this patient age-group. On this task, I predicted intact confidence estimates but excessive updating of choices following prediction errors in the adolescent OCD group, in line with findings in adult OCD patients. Unexpectedly, I found that adolescent patients only updated choices excessively when prediction errors were low. In other words, even when the coin did not deviate far from the last position, patients still updated the location of the bucket used for catching the coin. I speculated that these unnecessary updates were being driven by possible ‘not-just-right’ perceptions experienced by adolescent patients wherein they wanted to ensure the coin landed with high certainty into the bucket. Unlike past experimental chapters of this thesis showing abnormal performance by the medicated OCD group, I found that excessive updating following low prediction error magnitudes was mainly displayed by medication-naïve patients. This suggests that ‘not-just-right’ perceptions are perhaps remediated by SSRIs. Another significant finding from this chapter was that adolescents with OCD did not update their confidence ratings as much as controls following prediction errors. This is consistent with recent

research showing confidence ratings are not reduced following negative feedback in individuals with obsessive-compulsive traits (Rouault et al., 2018; Seow & Gillan, 2020). This suggests, overall, that actions and confidence are not influenced by negative prediction errors. I speculate that perhaps adolescent patients update their actions and beliefs according to an internal sense of 'incompleteness' or 'feelings of wrongness', in line with heightened error-related negativity and not-just-right perceptions in this population. Despite these abnormal results when assessing action and confidence separately, the formal regression analysis assessing the strength of action-confidence coupling revealed no differences between patients and controls. This could be due to patients' excessive action updating only being present when prediction errors were small, and not throughout the task. Hence, currently there is no clear evidence to support an action-confidence dissociation in adolescents with OCD.

In the final experimental chapter (Chapter 6), I aimed to assess probabilistic reversal learning in adolescents with OCD and investigate latent processes underlying learning and decision-making on this task. The experiment reported in this chapter employed the largest sample of participants out of all chapters, namely 50 adolescents with OCD and 53 healthy controls. Group difference results on this task were striking: adolescents with OCD displayed significant underperformance following reversal but intact acquisition learning. Intriguingly, computational modelling revealed that adolescents with OCD displayed heightened exploration (similar to findings from Chapter 4), reduced perseveration, increased reward learning rates, and reduced punishment learning rates compared to healthy controls. Reduced choice consistency here is in line with contemporary computational research reporting similar findings in adults and adolescents with OCD (Apergis-Schoute et al., in-prep; Hauser et al., 2017; Kanen et al., 2019). As in Chapter 4, increased exploration is once again speculated to be driven by patients' heightened feelings of uncertainty, reduced ability to arbitrate between exploitative and exploratory strategies, and possibly even impaired representation of choice values, leading to more sampling of alternative choices to accumulate evidence. Adolescent patients showing differential feedback learning (updating choice values more following rewards and less from punishment) is a novel finding, and supports the notion from Chapter 3's PIT data that adolescents with OCD are in fact not abnormally sensitive to punishment. In fact, here they appear to be significantly less driven by punishing feedback, which is in line with their blunted confidence updating to prediction errors from Chapter 5. In addition, this is the only experiment not to show an effect of medication status, suggesting that deficits are stable in adolescent-OCD regardless of treatment administration. The results in this chapter are indicative of atypical learning, decision-making, and feedback processing in adolescents with OCD.

7.2 Why do adolescents with OCD show apparently abnormal exploration?

Collectively from these findings, I infer that adolescents with OCD show a bias for exploratory decision-making when tasks are probabilistic, i.e. in Chapters 4 and 6. On deterministic tasks, such as the WCST in Chapter 2, decision consistency is equivalent between groups. This suggests that the extent to which value-guided decision-making is employed by adolescents with OCD depends on whether choice outcomes are stochastic or deterministic. This is convergent with research that reports that decision-making under uncertainty is abnormal in adults with OCD (Pushkarskaya et al., 2015; Zhang et al., 2015). In addition, Apergis-Schoute et al. (in-prep) administered deterministic and probabilistic reversal tasks to adults with OCD and found more habitual responding on the former but increased exploration on the latter. Hence, outcome stochasticity appears to modulate the extent to which exploratory heuristics are employed by adults and adolescents with OCD. However, it is ambiguous whether exploratory decision-making is truly associated with the disorder as OCD severity did not correlate with a tendency for exploration in Chapter 6. Symptom severity, on the other hand, was associated with exploration on the sequential decision-making task in Chapter 4, but only when considering all participants and not when observing only participants with OCD. Hence, the relevance of exploration to the clinical manifestation of OCD in adolescence is tentative at best, although there is more evidence for reduced perseveration to be linked to symptom severity in adult patients (Apergis-Schoute et al., in-prep; Kanen et al., 2019).

As mentioned briefly in the discussion section of Chapter 6, research into the explore-exploit dilemma has identified two forms of exploration. First, directed exploration involves weighing known choice values and choosing a novel option to improve pre-existing knowledge of all options present in an environment. Picture a scenario where you are deciding on which new restaurant to have dinner at. Directed exploration would entail thoroughly weighing the pros and cons of each possible restaurant before making an informed decision. Inversely, random exploration is not based on known choice values and reflects behaviour variability in decision-making. In the restaurant scenario, a random explorer would decide on a restaurant by tossing a coin.

Directed strategies are optimal in that they ensure the greatest amount of reward in the long-term, but they are cognitively taxing to execute. Random strategies, on the other hand, can perform ‘well-enough’ at the fraction of computational cost, as they still enable exploration of novel choices that may turn out to be rewarding (Wilson et al., 2014). Healthy adults have been found to engage in both forms of exploration to maximise their long term rewards (Findling, Skvortsova, Dromnelle,

Palminteri, & Wyart, 2019; Gershman, 2018; Wilson, Bonawitz, Costa, & Ebitz, 2020; Wilson et al., 2014), but children and young adolescents prefer to utilise random exploration (Dubois et al., 2020) likely due to the strategy being the simpler of the two.

It is uncertain in this current thesis whether the exploratory tendencies observed in adolescents with OCD are directed or random, or perhaps driven by some other unmodelled process. Other studies have just begun to understand how exploratory strategies differ as a function of psychiatric condition. For instance, patients with psychosis have been found to use directed strategies less than healthy controls but showed normal levels of random exploration (Waltz, Wilson, Albrecht, Frank, & Gold, 2020), whereas ADHD traits in healthy children is reportedly associated with increased random exploration (Dubois et al., 2020). Authors of these studies have attempted to draw conclusions from these findings, namely that reduced directed exploration is a reflection of poor goal-directed control in patients with psychosis, while random exploration in ADHD is thought to be linked to impaired attention and increased impulsivity. It is important that future studies also consider 1) the type of exploration patients with OCD engage in (e.g. more random exploration?), and 2) the factors driving this behaviour. The cognitive tasks presented in this thesis were unfortunately not designed or optimised for testing competing explanations for exploration, so these important questions remain unanswered for now. Nevertheless, the remainder of this section will attempt to underscore some possible mechanisms contributing to the supposed exploration bias displayed by adolescents with OCD.

7.2.1 The Bayesian brain theory: weak reliance on prior evidence

A popular computational framework to describe the machinations of the human brain is known as the Bayesian brain theory (Knill & Pouget, 2004). In this framework, the brain is posited to always be making inferences about hidden or latent causes of data being picked up by human senses (for example, hearing a sudden unusual loud noise). It does this by combining prior beliefs about the world using past experiences (‘this sounds similar to something else I’ve heard before’) and current sensory evidence accumulated in real-time (‘which direction is it coming from?’, ‘how loud is it?’), to generate possible reasons for a current experience (‘it is probably the sound of a truck backing up outside’). Based on this, a recent theoretical model of OCD suggests that intrusive worries and compulsions are a consequence of an inability to rely on prior experiences and outcomes as credible sources of information, leading to more reliance on sensory information (Fradkin, Adams, et al., 2020). As not all useful information is being taken into account, as it would be in a healthy Bayesian

brain, patients have difficulty predicting how different actions lead to different outcomes. Hence, they live in a constant state of uncertainty and conduct repetitive rituals in a futile effort to quell their feelings of doubt (e.g. repeatedly checking locks and switches). Furthermore, an inability to synthesise prior experiences means patients cannot rely on information gathered from past checking episodes to reduce uncertainty. Instead, an overreliance on sensory feedback, such as feelings of worry, doubt, and incompleteness, makes patients constantly feel that their actions were performed incorrectly. Concretely, a computational study recently revealed promising evidence for this model, wherein subjects with obsessive-compulsive traits displayed more uncertainty regarding actions and outcomes and had increased difficulty in relying on learnt contingencies which impaired their ability to predict future feedback (Fradkin, Ludwig, et al., 2020).

A combination of weak prior evidence and overreliance on sensory information can account for some of the exploration findings in my thesis. First, an inability to accurately formulate how actions form outcomes from previous experience, mistrust of gathered pay-off information, and heightened uncertainty, may have driven decisions that are not consistent with choice values, culminating in what appears to be exploration in Chapters 4 and 6. Moreover it may even account for other findings. In Chapter 5, adolescents with OCD may have revealed constant action updating despite low prediction errors as well as blunted confidence updating because they do not take into account external information provided by the predictive-inference task. Instead, they may be making choice updates based on internal sensations of 'wrongness', consistent with abnormally heightened ERN signals in this population. Further evidence that confidence in OCD is not dependent on external evidence can be found in Chapter 3, where the OCD group reported lower confidence ratings in memory of CS-US associations but were able to conduct specific and general transfer to the same extent as controls on the PIT task.

The model can also account for past studies revealing that paediatric patients spend too long accumulating evidence in decision-making tasks (Erhan et al., 2017; Hauser, Moutoussis, et al., 2017), supposedly due to their inefficiency in synthesising evidence throughout the duration of the task. Moreover, the model also suggests that young OCD patients display slow and impaired planning (Huyser et al., 2010; Kim et al., 2018; Negreiros et al., 2019) as a result of sensory feedback reporting that actions were not performed ‘correctly’ and an inability to synthesise prior information to plan for future actions.

Nonetheless, there are some findings I have reported in this thesis that Fradkin, Adams et al.’s model does not account for. First of all, Fradkin, Adams et al. (2020) propose that in some cases

patients with OCD prefer to use habit-directed over goal-directed policies, particularly when outcomes are more stable, because their uncertainty surrounding actions and outcomes makes it harder to predict outcomes from goal-directed strategies. Hence, Fradkin, Adams et al. suggest that it is easier for patients to rely on habit-based policies that have worked well in the past and are supposedly more reliable. This can account for findings of habitual responding in adults with OCD on tasks that are deterministic (Apergis-Schoute et al., 2017; Gillan et al., 2015, 2014, 2011), but the adolescents with OCD in my thesis displayed no evidence of habitual responding on the WCST in Chapter 2. Instead, the only impairment uncovered on the task was slower responding and increased unique errors by medicated patients, which may correspond more to disrupted attention in this group. Findings from the PIT task in Chapter 3 and the sequential decision-making task in Chapter 4 also suggest that model-free/habitual policies are not employed more by adolescent patients compared to controls. However, the model is able to account for why the adolescent patients are impaired on probabilistic compared to deterministic tasks such as the WCST, as the former contains more action-outcome uncertainty which makes learning reward contingencies over time more difficult for adolescent patients.

Next, Fradkin, Adams et al. (2020) also suggest that patients with OCD are unable to efficiently synthesise prior information. Instead, their actions are driven more by recently acquired feedback on cognitive tasks. This is indeed the case in adults with OCD (Vaghi, Luyckx, et al., 2017), yet in this thesis adolescents with OCD showed no evidence for heightened feedback sensitivity on any tasks employed with the exception of increased reward rates in Chapter 6, although this was coupled with decreased punishment rates. Additionally, in Chapter 5, increases in prediction error magnitude (equivalent to increasing the magnitude of punishing feedback) on the predictive-inference task, did not incur more action updating in adolescents with OCD, whom only showed excessive updating compared to controls following low prediction errors. As mentioned above it may be that adolescents with OCD are simply responding based purely on internal sensations (discomfort, incompleteness, doubt, etc), perhaps to a greater extent than adults with OCD whose choices are still influenced by external recent feedback.

Therefore, this framework can account for a large proportion of findings reported in this thesis, in particular findings pertaining to reduced choice consistency/exploration, but not all.

7.2.2 Choice value sensitivity and evidence accumulation

Literature into the explore-exploit dilemma posit that an exploratory strategy is beneficial when environments are volatile, as it facilitates sampling from novel options and enables maximisation of

rewards in the long-term (as opposed to exploitation which only enables short-term reward maximisation) (Addicott et al., 2017). However, adolescents with OCD do not appear to be using exploration as a cognitive strategy as they show both increased exploration and impaired performance on the probabilistic reversal learning task (Chapter 6). Thus, perhaps their exploratory behaviour can be reformulated as an impairment in value-guided decision-making. Indeed, it has been hypothesised that frequent choosing of inferior options may be the result of noisy or inaccurate representations of choice values instead of exploration (Pedersen et al., 2017). All published studies showing exploration/reduced perseveration in patients with OCD (e.g. Kanen et al., 2019; Hauser et al., 2017) do not use models, such as RL-DDM, that tap into the extent to which subjects can discriminate between competing choices based on their values. Based on findings from studies showing action-outcome representations are faulty in people with compulsive traits (Fradkin, Ludwig, et al., 2020; Seow et al., 2020), it may very well be the case that patients with OCD have faulty knowledge of choice values in reinforcement learning tasks. Hitherto, OCD research has mostly fit drift-diffusion models to data from perceptual decision-making tasks such as the Dot Motion Discrimination task that requires participants to report whether a large group of dots on screen are mostly moving to the left or right on screen. In general, these drift-diffusion studies report that patients with OCD have lower drift rates, meaning they make slower and less accurate decisions as they are unable to discriminate effectively between the two competing options (Banca, Vestergaard, et al., 2015; Erhan et al., 2017; Mandali et al., 2019). However, these studies do not utilise reinforcement learning models alongside drift-diffusion models which means they cannot investigate crucial learning mechanisms, such as feedback sensitivity, that are captured in RL models.

In this thesis, I was able to probe this poor choice value representation theory in Chapter 4 where I fit an RL-DDM to data from a sequential decision-making task. Contrary to what was expected, there were no significant group differences in the drift rate scaling parameter used, but patients did make more exploratory responses and also displayed lower boundary separation parameter values indicating they favoured speed over accuracy. The lack of difference in drift rate scaling values suggest patients with OCD are aware of choice values to the same extent as control subjects, but they seemed to ignore these values when making decisions. In the discussion of Chapter 4, I speculated that patients made more erratic choices because the task trials were timed, and adult patients with OCD have been found respond fast and gather less evidence when penalised for slowness (Banca et al., 2015). As a result of this erratic responding, it may have been difficult to determine whether patients could actually differentiate between choice values or not. Adding to this, exploration in OCD patients on this task correlated with drift rate scaling values but not boundary separation values,

indicating that exploration displayed by adolescents with OCD is associated with lower discrimination between choice values. To study the relationship between drift rates and exploration further, it may be crucial to fit the RL-DDM to data from tasks that are self-paced in future studies.

7.2.3 Role of learning and memory

Reduced value-guided decision-making in adolescents with OCD could be attributed to an impairment in learning values associated with choices in the first place, or perhaps a deficit in storing representations of multiple choice values in memory. This would be consistent with findings from Gottwald et al. (2018) who reported that adolescents with OCD displayed marked deficits on various learning and memory tasks. However, adolescents with OCD in my thesis did not show as pronounced a learning deficit as was reported in Gottwald et al.'s study. For instance, adolescent patients in my experiments were able to perform with the same accuracy as control subjects on the WCST (Chapter 2), learn US-response and CS-US associations sufficiently to conduct specific and general transfer on the PIT task (Chapter 3), muster model-based control to the same extent as healthy adolescents (Chapter 4), and respond similarly to controls on the predictive-inference task when prediction error magnitudes were not low (Chapter 5). Some evidence of a learning impairment in adolescents with OCD was found on the probabilistic reversal learning task in Chapter 6 where patients' performance worsened post-reversal. Albeit, pre-reversal learning was intact in my sample of adolescents with OCD which contrasts with Gottwald et al.'s adolescent OCD participants displaying poor rule learning on the ID/ED task and poor instrumental learning on an outcome devaluation task. Results from Chapter 6 suggest that patients' learning only becomes disrupted when there are changes in outcome contingencies, which points to an issue in coping with environmental volatility (Pushkarskaya et al., 2015) and not a pure learning problem.

Concerning a potential memory deficit, a recent study employing a modified Dot Motion Discrimination task where subjects had to make decisions and then repeat their decisions later on, found that adults with obsessive-compulsive (OC) traits had impaired implicit memory for first decisions which led to reduced drift rates (less efficient evidence integration/reduced choice value sensitivity) when repeating decisions (Solway, Lin, & Vinaik, 2020). Those authors suggest that impaired implicit memory for past actions leads to poor repetition of these actions in the future, which may account for reduced choice consistency in adolescents and adults with OCD. However, they also found that drift rates were already significantly decreased when high OC subjects made their initial decisions, and this deficit cannot be explained by impairments in implicit memory. Hence, some other process may be impacting patients' disrupted evidence accumulation.

In this thesis, I had no measure of implicit memory but I used the digit span assessment as a test of both verbal memory (forwards digit span) and working memory (backwards digit span), and found no differences between OCD and control participants on these measures. Memory was not formally tested on any of the cognitive tasks in this thesis, with the exception of the PIT task in Chapter 3 which probed whether participants were able to remember associations learnt from the Instrumental and Pavlovian learning phases during the PIT phase. Medicated patients showed a tendency to misremember CS-US pairs during the Pavlovian phase and also reported reduced memory confidence, but this did not impact their ability to conduct specific and general PIT later on. Nonetheless, these results are unsurprising as it has already been established in the literature that patients with OCD are not impaired on digit span tasks (see Chapter 1). Instead, memory impairments may be most prominent on non-verbal, visuospatial tasks, for example adolescent patients have been found to be impaired on the Paired Associates Learning task (Sahakian et al., 1988) administered in Gottwald et al.'s (2018) study. Although, other studies probing visuospatial non-verbal memory in youths with OCD report no impairment (Beers et al., 1999; Chang et al., 2007; Geller et al., 2018; Hybel et al., 2017; Kim et al., 2018; Shin et al., 2008) – see Chapter 1. Hence, poor memory representation of choice values (which taps into non-verbal memory) may still be present in adolescents with OCD, leading to more inaccurate responding, but this must be directly probed in further studies.

In summary, findings from this thesis do not support the hypothesis that learning or working memory are significantly impaired in adolescents with OCD. Instead, patients appear to show disrupted behavioural performance following changes in contingencies indicating an issue coping with uncertainty or environmental volatility. However, there is the possibility that implicit and/or non-verbal memory deficits resulted in poor choice value representation, which collectively led to reduced decision accuracy, but this notion needs to be researched in future work.

7.2.4 Anxiety and Stress

Group differences reported in this thesis might even be the result of factors not directly linked to OCD. Despite having no comorbid diagnoses, adolescents with OCD still showed elevated anxiety and depression scores than healthy controls. First, regarding anxiety, intolerance of uncertainty is also a characteristic of individuals with anxiety disorders (Holaway, Heimberg, & Coles, 2006; Meyer, 2017). Additionally, heightened ERN is a shared trait of anxiety and obsessive-compulsive disorders (Riesel, 2019). Therefore, the anxiety or stress participants feel when outcome contingencies change could be contributing to their less accurate and more random responding in Chapters 2, 4, and 6. Supporting this, acute stress triggered in healthy volunteers is found to impair

learning and decision-making (Porcelli & Delgado, 2017; Wemm & Wulfert, 2017) while youths with clinical anxiety are reported to make less correct responses post-reversal during a probabilistic reversal learning task (Dickstein et al., 2010).

Computational modelling research has also uncovered findings in individuals who are stressed or anxious that parallel how adolescents with OCD update choice values from feedback in Chapter 6. Inducing acute stress reportedly improves learning from positive outcomes but impairs learning from negative outcomes (Lighthall et al., 2013; Mather & Lighthall, 2012; Ting et al., 2020). Stress perhaps biases individuals to be reward sensitive, possibly because they are motivated to seek outlets that can reduce stress (Mather & Lighthall, 2012; Sinha et al., 2009). Indeed, adolescents with OCD in Chapter 6 also revealed heightened reward learning rates and reduced punishment rates compared to healthy controls.

Nonetheless, the reinforcement learning literature involving stress/anxiety is highly varied as stress has also been found to reduce reward processing while increasing punishment processing (Berghorst, Bogdan, Frank, & Pizzagalli, 2013; Mkrtchian, Aylward, Dayan, Roiser, & Robinson, 2017). Another study, conversely, reported no evidence of atypical reward or punishment learning in anxious individuals but found evidence for poor learning overall (LaFreniere & Newman, 2019). Hence, it is difficult to determine whether decision-making displayed by adolescents with OCD in this thesis truly mirrors that of stressed or anxious individuals. In addition, none of the studies cited here reported increased exploration or reduced perseveration in the anxious sample, suggesting that these key behaviours are unique to OCD.

When conducting correlation analyses per chapter in this thesis, it was found that anxiety scores combined with OCI scores predicted fewer correct responses on the probabilistic reversal learning task in Chapter 6 and more exploration on the sequential decision-making task in Chapter 4, suggesting a possible influence of anxiety on task behaviour. However, these correlations ceased to be significant when conducting the analyses within OCD and control groups, suggesting that anxiety is not driving this abnormal decision-making in adolescents with OCD. Adding to this, anxiety scores were unrelated to task measures reported in Chapters 2,3, and 5.

7.2.5 Depression and Anhedonia

Instead of anxiety, adolescent patients' elevated depression symptoms may have influenced their decision-making instead. A characteristic of Major Depressive Disorder (MDD) is anhedonia which describes a loss of interest, pleasure, and motivation in tasks or activities. Significant anhedonia is found to be expressed in adult patients with OCD and their first-degree relatives (Xu et al., 2020).

Hence, depressive feelings and anhedonia experienced by adolescents with OCD could have potentially reduced their motivation to make value-guided decisions on the probabilistic tasks. However, many studies investigating reinforcement learning in populations with MDD find no significant impairments when employing both frequentist analyses and computational modelling (Brolsma et al., 2020; Chase et al., 2010; Dickstein et al., 2010; Remijnse et al., 2009). To my knowledge, only one study has revealed that patients with MDD showed reduced reward learning rates compared to healthy controls (Mukherjee, Filipowicz, Vo, Satterthwaite, & Kable, 2020), while my adolescent patients showed the opposite result in Chapter 6.

Next, regarding exploration, one study reported that MDD patients do not make more exploratory choices compared to healthy controls (Cella, Dymond, & Cooper, 2010), which is once again at odds with my findings in adolescents with OCD. Although, one study has found that healthy young adults with depressive traits made more exploratory choices on a two-armed bandit task (Blanco, Otto, Maddox, Beevers, & Love, 2013). However, this study did not account for anxious or obsessive-compulsive symptoms in the group with depressive traits. Overall, it is not certain whether exploration displayed by adolescents with OCD can be attributed to their depressive symptoms.

Correlational analyses per chapter in this thesis revealed that depression scores intriguingly predicted improved performance in participants, namely less perseverative errors on the WCST in Chapter 2, increased drift rate scaling values within controls in Chapter 4, and decreased learning rates on the predictive-inference task in Chapter 5. This indicates that atypical decision-making displayed by adolescents with OCD are unlikely to be driven by symptoms of depression.

Recently, dimensional research has revealed that impaired decision-making performance is strongly associated with obsessive-compulsive traits but not anxious or depressive traits, and that this impaired performance is mediated by a tendency for more exploratory decisions (Suzuki, Yamashita, & Katahira, 2019). This offers firm evidence for abnormal exploration being a characteristic of OCD and not anxiety or depression.

7.2.6 Motor Disinhibition and Impulsivity

An alternative explanation for choice randomness seen in Chapters 2 (as increased unique errors on the WCST may be attributed to random responding), excessive exploration in Chapters 4 and 6, as well as unnecessary action updating in Chapter 5 is that adolescents with OCD are impaired at inhibiting inappropriate motor actions, which may be analogous to impulsivity. Evidence for this stems from research reporting that brain regions linked to motor actions, including the supplementary motor area (SMA) and pre-SMA, are over-recruited in adults with OCD (De Wit et al., 2012; Norman

et al., 2019; Yücel et al., 2007). In addition, adults with OCD reportedly display increased readiness potential signals (Morand-Beaulieu, Aardema, O'Connor, & Lavoie, 2020), which is the brain signal representing motor preparedness and the decision to initiate movement (Kornhuber & Deecke, 2016). These heightened signals are likely to influence adult OCD patients' inability to inhibit pre-potent responses on motor inhibition tasks (Chamberlain, Fineberg, Menzies, et al., 2007; Chamberlain, Müller, et al., 2006; Menzies et al., 2007; Penadés et al., 2007). In the context of the current findings, motor disinhibition may be driving random choices and frequent action updating displayed by adolescents with OCD. More convincingly, activation in the pre-SMA is associated with more exploratory decision-making (Laureiro-Martínez et al., 2015) suggesting a neural basis for patients' over-exploration.

Similarly, adolescent patients' choice randomness could be attributed to impulsivity, which describes the tendency to display behaviour with little forethought or consideration of consequences. Supporting this, attention deficit hyperactivity disorder (ADHD) and OCD are often comorbid in childhood (Brem, Grünblatt, Drechsler, Riederer, & Walitza, 2014) and children with ADHD and OCD share similar patterns of abnormal frontal cortex activity during decision-making (Christina O. Carlisi et al., 2017; Norman et al., 2018; Norman et al., 2017). In addition, the ERN which is found to be reliably increased in youths with OCD is also reported to be a marker for impulsivity in adolescence (Taylor, Visser, Fueggle, Bellgrove, & Fox, 2018). Furthermore, random exploration (Dubois et al., 2020) and reduced inhibition (Wodka et al., 2007) are reported to be associated with ADHD traits. Hence, there is a possibility for impulsivity/ADHD traits to be driving decision-making in the current OCD sample, but no impulsivity questionnaires were administered in the experiments of this thesis so this cannot be confirmed at present.

However, children with OCD largely show no deficits on behavioural inhibition tasks as highlighted in Chapter 1 (Andrés et al., 2007; Beers et al., 1999; Chang et al., 2007; Garcia-Delgar et al., 2018; Geller et al., 2018; Gooskens et al., 2018; Gruner et al., 2012; Ota et al., 2013). In addition, there is a lack of evidence for increased SMA and pre-SMA activity in paediatric OCD patients compared to the literature in adult OCD. In fact, one study actually reported reduced pre-SMA activity in paediatric OCD patients compared to healthy children (Rubia, Cubillo, Woolley, Brammer, & Smith, 2011). Thus, there is not enough evidence to ascertain whether motor inhibitory deficits are present in adolescent patients, and whether this drives their reduced value-guided decision-making.

7.2.7 Neural Basis for Abnormal Exploration

As alluded to in Chapters 4 and 6, neuroimaging evidence also offers insight into abnormal exploration or reduced value-guided decision-making in OCD. In healthy people, the ventromedial prefrontal cortex (vmPFC) is thought to show differential activation for exploitative (Daw et al., 2006; Laureiro-Martínez et al., 2015) and exploratory actions (Domenech et al., 2020; Trudel et al., 2020), indicating the importance of the vmPFC in arbitrating between the different strategies. In parallel, the dACC has been found to be active only during exploratory choices (Kolling, Behrens, Mars, & Rushworth, 2012; Laureiro-Martínez et al., 2015; Trudel et al., 2020). The dACC is thought to be implicated in behavioural monitoring and adaptation, and to trigger the search for better alternatives when making decisions (Kolling et al., 2012; Kolling, Scholl, Chekroud, Trier, & Rushworth, 2018). More recently, dACC activity was associated with decisions that deviated from choice values, indicating the importance of the area in value-independent decision-making (Findling et al., 2019). The vmPFC (Apergis-Schoute et al., 2018; Fitzgerald et al., 2018, 2010; Huyser et al., 2011; Stern et al., 2011, 2013) and dACC (see Riesel et al., 2019 and Marzuki 2020 for reviews) are consistently reported to be overactive in OCD, suggesting abnormalities present in the OCD brain system responsible for arbitrating between exploratory and exploitative decision-making. In particular, overactive vmPFC activation is associated with poor safety learning and increased uncertainty in adults with OCD (Apergis-Schoute et al., 2017; Stern et al., 2013), while a plethora of research has identified elevated ACC signals associated with errors in both children and adults with OCD (e.g Carrasco et al., 2013; Chamberlain & Menzies, 2009; Riesel, Endrass, Kaufmann, & Kathmann, 2011; Riesel, Kathmann, & Endrass, 2014). Heightened activity in these regions under specific contexts imply patients constantly feel they are under threat or are underperforming, and perhaps feel the need to change their behaviour in order to cope. Nonetheless, research has yet to determine whether abnormal vmPFC and ACC activation are directly associated with increased exploration in OCD. Future work should focus on understanding brain systems underlying maladaptive exploration in OCD, which is recently emerging as a major cognitive feature of the disorder.

Summary

In this section I have highlighted that exploration or reduced value-guided decision-making during tasks with probabilistic choice pay-offs is a prominent feature of adolescent OCD. I discuss evidence for and against various factors potentially contributing to these results, namely weak reliance on information accumulated over time and stronger reliance on internal sensations when making inferences, poor representation of values associated with choices, impairments in learning and

remembering choice values, enhanced depressive and/or anxious traits, motor impulsivity, and lastly a deficit in disengaging from exploratory decision-making supported by work reporting abnormal vmPFC and ACC activity in OCD. These explanations are speculative for now and future research employing well-designed tasks that can probe exploratory behaviour under different conditions alongside neuroimaging techniques is necessary to uncover why exploration is abnormal in OCD. Promisingly, several studies have already successfully teased apart random, noise-driven exploration from information-seeking exploration in healthy subjects using specific paradigms and sophisticated models (Dubois et al., 2020; Findling et al., 2019; Wilson et al., 2020, 2014). Perhaps such models and tasks can be employed to thoroughly investigate exploration in populations with OCD.

7.3 Neurocognitive distinctions between adolescent-OCD and adult-OCD

In each experimental chapter of this thesis, most hypotheses were formulated based on adult OCD research, as the child/adolescent-OCD cognitive literature is sparse. Through this, I was able to obtain insight into how learning and decision-making in adolescent OCD compares to adult OCD. The main similarity uncovered was that adolescents with OCD display exploratory decision-making and reduced perseveration during probabilistic tasks which is also reported in adults with OCD (Apergis-Schoute et al., in-prep; Hauser et al., 2017; Kanen et al., 2019), suggesting that these features are stable across the lifespan in OCD. However, adolescents with OCD also expressed attributes that are distinct from typical findings in adults with OCD which will be discussed in detail here.

The most conspicuous departure from the adult OCD literature is that adolescents with OCD showed no evidence of a cognitive flexibility deficit (Chapter 2), and furthermore showed equivalent model-based/goal-directed reasoning to participants without OCD (Chapters 3 and 4). First, the lack of cognitive flexibility deficit found in Chapter 2 as well as in past paediatric OCD studies is striking as cognitive inflexibility is considered a potential endophenotype of OCD (Chamberlain & Menzies, 2009) as adults with OCD and unaffected first-degree relatives also display this behaviour (Cavedini et al., 2010; Chamberlain, Fineberg, Menzies, et al., 2007; Menzies et al., 2007). Moreover, cognitive inflexibility corresponds well to patients' tendency for producing persistent and repetitive obsessions and compulsions. In fact, a recent meta-analysis found that cognitive inflexibility on the ID/ED task is a robust trait of adult OCD (Chamberlain et al., manuscript submitted), although these findings are challenged somewhat by a separate meta-analysis showing that impairments on set-shifting tasks in

this population are broad and not limited to inflexibility and habitual responding (Fradkin et al., 2018).

Next, comparable model-based reasoning between adolescents with OCD and healthy adolescents indicates an absence of maladaptive habit formation as well as intact goal-directed control in adolescent-OCD which is inconsistent with findings in adult OCD (Apergis-Schoute et al., 2017; Gillan et al., 2014, 2011). Moreover, this conflicts with Gottwald et al.'s (2018) findings showing that adolescents with OCD display reduced goal-directed control on outcome devaluation tasks. These findings run counter to the 'habit hypothesis' (which postulates that a bias for habit formation over goal-directed behaviour drives compulsive tendencies) as a possible cognitive model of compulsivity. After all, if an overreliance on habits is absent in young patients, it is unlikely to be the reason for compulsions in both adolescent- and adult-OCD. Moreover, a longitudinal study showed that compulsive tendencies are predictive of reduced model-based reasoning in healthy adolescents (Vaghi et al., 2020), suggesting disrupted goal-directed faculties to be a consequence rather than a cause of compulsions in OCD.

Next, adolescents with OCD revealed no significant action-confidence dissociation compared to healthy adolescents in Chapter 5, despite robust evidence for adults with OCD and adults with obsessive-compulsive traits presenting a disconnect between actions and beliefs (Rouault et al., 2018; Seow & Gillan, 2020; Vaghi et al., 2019; Vaghi, Luyckx, et al., 2017). Intact action-belief association strength in adolescents with OCD has also been reported in a past study (Gottwald, 2017, thesis), implying that the two constructs perhaps become unlinked with age or as disorder duration increases. Similar to the habit hypothesis, a disconnect between action and meta-cognition has been labelled a promising neuropsychological mechanism underlying compulsive behaviour (Vaghi, Luyckx, et al., 2017) due to the ego-dystonic nature of the disorder. Gottwald's and my findings indicate that this model may not be compatible with juvenile-OCD. Nonetheless, findings from my thesis provide evidence for abnormalities in meta-cognition alone in adolescents with OCD, namely reduced confidence updating following prediction errors in Chapter 5, and decreased memory confidence in CS-US associations in Chapter 3. This suggests that changes in meta-cognition displayed by adolescents with OCD are domain dependent by which confidence in decision-making is resistant to unexpected outcomes while confidence in memory is generally reduced. The distinction between meta-decision-making and meta-memory is consistent with research in adult OCD (Boschen & Vuksanovic, 2007; Hermans et al., 2008; MacDonald et al., 1997; Rouault et al., 2018; Seow & Gillan, 2020; Tolin et al., 2001). These findings suggest that meta-cognition is not a unitary phenomenon and moreover, there is evidence for distinct brain regions underlying confidence in

decision-making versus memory (Fleming, Ryu, Golfinos, & Blackmon, 2014). I speculate that individuals with OCD are relatively confident in their decisions as they are being made in real-time, since tasks that probe meta-decision-making require that subjects rate their confidence trial-by-trial. In contrast, paradigms probing meta-memory often ask that subjects rate how confident they are in their memories after completing a task. Patients with OCD perhaps express more doubt in their abilities after completion of a task or ritual but not during. Perhaps as a result of difficulty in accumulating and synthesising past information (Fradkin, Adams, et al., 2020) patients with OCD distrust their memories of rituals completed in the past leading to increased repetition of rituals in the present.

Lastly, my findings contradict the harm avoidance model of OCD which proposes that compulsions are conducted to prevent incoming danger, harm, or unpleasant thoughts (Rasmussen & Eisen, 1990, 1992), as there was no evidence of excessive punishment sensitivity or harm avoidance in adolescents with OCD across all studies conducted in this thesis. Concretely, adolescent patients revealed reduced punishment learning rates during probabilistic reversal learning, even though studies employing adult OCD samples do not report abnormalities in learning rates (Apergis-Schoute et al., in-preparation; Hauser et al., 2017; Kanen et al., 2019). In addition, adolescents with OCD did not display significantly increased avoidance responses under extinction during the PIT task in Chapter 3, even though adults with OCD have been found to be highly harm avoidant on aversive deterministic learning paradigms, where they display excessive avoidance responses to devalued stimuli (Apergis-Schoute et al., 2017; Gillan et al., 2014).

7.3.1 Possible explanations for differences between adults and adolescents with OCD

There are several factors that may contribute to the distinctions in findings between adults and adolescents with OCD. One obvious factor may be that cognition perhaps declines as disease duration prolongs, suggesting that most cognitive impairments associated with OCD are not causally linked to the disorder. Additionally, other factors such as the heterogeneity in treatments received over the years, negative life experiences due to the disorder, and comorbid psychiatric disorders developed over the lifetime may also shape cognition in adults with OCD. This demonstrates the importance of studying paediatric samples of OCD as it allows for a relatively untampered window into the early cognitive characteristics associated with the disorder.

Despite these cognitive distinctions, several reviews have concluded equivalent altered brain activity between paediatric and adult OCD patients (Brem et al., 2012; Maia, Cooney, & Peterson,

2008; Marzuki et al., 2020; Norman et al., 2016), specifically in regions within the cortico-striato-thalamo-cortico loops including the OFC, ACC, PFC, and basal ganglia. Perhaps dysfunction starts off predominantly neural in adolescent patients but eventually culminates in cognitive impairment later in life, for instance reduced ACC volume predicts future performance monitoring abnormalities and the development of OCD in young children (Gilbert et al., 2018). These findings imply that mechanisms contributing to OCD are more neurobiological than cognitive, which accounts for neural markers, such as ERN, being reliably abnormal in child and adult patients, but not cognitive markers.

Nonetheless, there is also evidence for brain differences between child and adult patients that may be contributing to these separate cognitive profiles. For instance, as described in Chapter 1, brain regions underlying habit-directed behaviour are overactive following symptom provocation in adults with OCD (Banca, Voon, et al., 2015), but underactive in children with OCD (Gilbert et al., 2009) which may explain the lack of excessive habitual responding in my sample of adolescents with OCD. Moreover, a review by Huyser et al. (2009) reported that differences between children and adults with OCD are more pronounced using structural compared to functional neuroimaging methods, suggesting that caution should be exercised when interpreting brain findings obtained from different neuroimaging modalities. Huyser et al. posited that paediatric OCD patients show more structural abnormalities in the globus pallidus and thalamus compared to adults who typically show structural OFC and caudate abnormalities. In particular, structural paediatric studies report that children with OCD show larger grey matter density in the OFC compared to age-matched controls (Szeszko et al., 2008) while adult studies often report bilateral reductions in OFC volumes in OCD patients (Atmaca, Yildirim, Ozdemir, Tezcan, & Kursad Poyraz, 2007; Atmaca et al., 2006; Hoexter et al., 2012; Rotge et al., 2009; Szeszko et al., 1999). Moreover, reduced caudate volume is seen in adults with OCD (Bartha et al., 1998; Ebert et al., 1997; Luxenberg et al., 1988; Robinson et al., 1995) but not in child patients (Maia et al., 2008; Rosenberg et al., 1997; Szeszko et al., 2004). Paediatric patients showing normal volumes in these areas may enable protection against certain types of cognitive deficit in, as the OFC is implicated in response inhibition (Elliott & Deakin, 2005; Hooker & Knight, 2010), while the caudate is reported to be one of the regions linked to cognitive flexibility in OCD (Vaghi, Vértes, et al., 2017). Conversely, a more recent meta-analysis has uncovered that adults and youth with OCD, in fact, have similar grey matter volumes in the striatum (enlarged) and PFC (reduced), but adult patients displayed smaller grey matter volumes in the ACC and greater grey matter volumes in the cerebellum compared to child patients (Hu et al., 2017). I speculate that perhaps paediatric brains develop to become similar to adult patients' brains over time, suggesting that disorder duration impacts brain structure as well as cognition. However, there is a shortage of longitudinal research

exploring how brain structure changes over the course of development in OCD patients, as well as neuroimaging research directly comparing child and adult patients. As a result, it is impossible at present to know whether these structural impairments are a consequence of OCD or vice versa, and whether child patients eventually acquire brain profiles matching those of adult patients with age. One cross-sectional resting state study has reported that children with OCD showed reduced connectivity from the dorsal striatum and thalamus to the rostral and dorsal ACC (Fitzgerald et al., 2011), which was absent in older adolescent and adult patients, providing some insight into how the brain develops with age in OCD. However, patient sample sizes in this study were small, with only 11 children and 18 adolescents compared to 31 adults. Neuroimaging research studying adults with early- onset vs late-onset OCD also show mixed results and utilise small subject samples (see Taylor et al., 2011 for review). In addition, there is an issue with interpretation of these resting-state and structural brain results, as it is uncertain how atypical functional and structural findings in OCD are directly associated with cognitive functioning.

As alluded to in several chapters, healthy adolescents may be showing age-related reduced performance across various domains as their neural and cognitive faculties are still developing (Giedd et al., 1999; Luna et al., 2001), which accounts for the lack of pronounced differences between adolescents with OCD and controls. Indeed, when compared to adults, *healthy* children and adolescents have been found to show reduced goal-directed/model-based reasoning (Decker et al., 2016), inaccurate meta-cognition (Fandakova et al., 2020; Moses-Payne, Habicht, Bowler, Steinbeis, & Hauser, 2020; Weil et al., 2013), and increased punishment sensitivity (Hauser et al., 2015; Rodriguez Buritica et al., 2019; Rosenbaum, Grassie, & Hartley, 2020; van den Bos et al., 2012). Although healthy older children and adolescents are thought to show similar performance to adults on cognitive flexibility tasks such as the WCST (Chelune & Baer, 1986). Thus, some impairments which are pronounced in adult OCD may arise due to disrupted development of cognitive functions as cognitive characteristics present in childhood do not fully mature with age. Empirical evidence for this was established in a longitudinal study showing that compulsions impair otherwise normal development of model-based control in healthy adolescents (Vaghi et al., 2020). Intriguingly, the same line of reasoning may apply to clinical symptoms of OCD as research suggests that ritualistic, compulsive behaviour is actually typical in young healthy children (Evans, Lewis, & Iobst, 2004). Childhood behaviours that are similar to symptoms of obsessive-compulsive spectrum disorders include rigid routines, strong preferences, rigid food habits, acute perceptions of minute flaws in toys or clothes, and perceptions of subtle changes in the environment. While maturation of neurobiological systems relevant for flexible behaviour (most prominently involving the OFC

region) leads to these behaviours being phased out over time in healthy development (Evans et al., 2004), the same behaviours instead are entrenched in OCD.

There is also the possibility that adult- and adolescent-OCD are different subtypes or even separate disorders altogether, which would account for the distinctions in clinical, cognitive, and neural presentation. One piece of evidence for this is that candidate endophenotypes of OCD including impaired cognitive flexibility and response inhibition, are present in adults with OCD and their probands but not in adolescents and children with OCD. As endophenotypes are meant to signal genetic risk for the disorder, it is unusual that they would not be present in young people with OCD. A few studies have pointed towards genetic differences between developmental subtypes, namely, higher heritability estimates are associated with paediatric OCD, and early-onset OCD is more likely than late-onset OCD to occur in first-degree relatives (Taylor, 2011; Van Grootheest et al., 2005). At the genetic level, differences in the serotonin transporter gene (SCL6A4) between adults and children/adolescents with OCD have been uncovered (Grünblatt et al., 2018). However, genetics cannot account for why adults with early onset OCD also show phenotypic differences from children and adolescents with OCD (Butwicka & Gmitrowicz, 2010; Sobin, Blundell, & Karayiorgou, 2000) as one would assume that both groups have the same genetic makeup. Moreover, most human genetic studies have been unable to quantify genes that are significantly linked to increased susceptibility for OCD (Pauls, 2008), suggesting more of an influence of environmental factors or an environment-by-gene interaction. Hence, it is likely that some combination of environmental factors, such as age of onset and disorder duration, and genetic factors interact to inform the highly heterogeneous clinical and cognitive presentation of OCD.

Nonetheless, there are some characteristics that fulfil endophenotype criteria for both children and adults with OCD, namely slower and impaired planning linked to reduced dlPFC activation (Lochner et al., 2020; Negreiros et al., 2019; Vaghi, Hampshire, et al., 2017), and increased ERN and performance monitoring (Riesel, 2019). This indicates some genetic and familial overlap between subtypes. Additionally, this suggests that these characteristics are stronger candidate endophenotypes of OCD than cognitive flexibility and response inhibition as they are present regardless of age-of-onset and disorder duration. Relevant to major findings in this thesis, future research should attempt to establish whether increased shifting/exploration on probabilistic reversal tasks qualifies as an endophenotype as we now know this characteristic is present in both adult and adolescent OCD populations.

Summary

Results of my thesis indicate that adolescents with OCD are similar to adult patients in that they show abnormal exploration and reduced perseveration on probabilistic learning tasks, and additionally show altered meta-cognition. This supplements past findings showing other similarities between subtypes (see Table 7.1 for summary). However, adolescent patients are also distinct from adult patients on other cognitive domains (see Table 7.1). Proposed reasons for these distinctions include prolonged disorder duration in adults with OCD, neural abnormalities preceding cognitive decline, structural and functional brain differences between paediatric and adult subtypes, and that OCD may be a disorder associated with disrupted maturation of cognitive functions present in childhood. There is also the possibility that child-OCD and adult-OCD are different subtypes of the disorder supported by endophenotype and genetic research, but important caveats should be considered.

Table 7.1: Summary of similarities and distinctions between adult and adolescent subtypes based on previous literature and findings from current studies in thesis.

	Adult-OCD	Adolescent-OCD
Cognitive inflexibility	✓	✕
Poor response inhibition	✓	✕
Slow and disrupted planning	✓	✓
Increased ERN and performance monitoring	✓	✓
Non-verbal and visuospatial memory	✓	Possibly
Reduced perseveration and more exploration on probabilistic tasks	✓	✓
Abnormalities in meta-cognition	✓	✓
Action-Belief dissociation	✓	Uncertain
Reduced goal-directed control	✓	✕
Heightened punishment sensitivity	✓ (During deterministic tasks)	✕

7.4 Effects of Medication

Most studies presented in this thesis report effects of medication, and the majority of these studies reveal significant atypical performance expressed by adolescent patients medicated with SSRIs, despite both medicated and unmedicated patients showing comparable ages, IQ scores, OCD severity, and anxiety and depression scores. Medicated patients 1) committed more unique errors and were slower on the WCST in Chapter 1, 2) made more errors when pairing USs with CSs and showed reduced memory confidence compared to controls in the Pavlovian phase of the PIT task in Chapter

3, and 3) favoured speed over accuracy and showed more exploration on the sequential decision-making task in Chapter 4. Conversely, unmedicated subjects showed abnormal performance on the predictive-inference task in Chapter 5 wherein they updated actions significantly more than control subjects, particularly when prediction errors were low. However, there was no effect of medication on the probabilistic reversal learning task in Chapter 6, despite this study employing the largest sample of medicated (n=30) and unmedicated (n=20) patients. Instead, all subjects with OCD displayed abnormal performance on this task regardless of medication status. This calls into question the medication effects reported in Chapter 2-5 as the sample sizes per group (after splitting the OCD group into MED+ and MED-) in these chapters were much smaller, suggesting effects may have occurred by chance. Nonetheless, it is still important to speculate other possible reasons for the medication effects uncovered in these chapters.

SSRIs operate by blocking the action of the serotonin transporter (5-HTT) protein which is responsible for the reuptake of intra-synaptic 5-HT (serotonin), which in turn promotes an increase of 5-HT concentration in synapses. In animal models, SSRIs are found to enhance activity in the OFC and caudate nucleus (Bergqvist, Bouchard, & Blier, 1999; Mansari, Bouchard, & Blier, 1995), which are regions that show aberrant activation during reversal learning and cognitive flexibility in patients with OCD (Chamberlain et al., 2008; Vaghi, Vértes, et al., 2017). Behaviourally, SSRIs are thought to re-engage these regions involved in goal-directed fronto-striatal circuits, enabling greater resistance against obsessions and compulsions (Palminteri et al., 2012). Indeed, administration of SSRIs has led to improvements in executive functions such as reversal learning in animals (Barlow et al., 2015; Clarke et al., 2007), reward and punishment learning in adults with OCD (Palminteri et al., 2012), as well as memory, inhibition, and cognitive flexibility in child-patients with OCD (Andrés et al., 2008). Unmedicated, but not medicated, patients performing abnormally in Chapter 5 is consistent with the demonstrated cognitive remediating effects of SSRIs in OCD, but it is curious that SSRIs appeared to promote more atypical performance in other chapters. My findings provide preliminary evidence for SSRIs to not be especially beneficial for cognition in adolescent-OCD.

As alluded to in Chapters 2-4, there is evidence for impaired learning and flexibility following acute low-dosage SSRIs administered to healthy volunteers (Chamberlain, Müller, et al., 2006; Skandali et al., 2018). Similarly, adolescent patients in this thesis on lower doses of SSRIs displayed lower IQ, and reduced model-based decision-making and reward sensitivity on the sequential decision-making task in Chapter 4. This indicates that administration of lower doses of SSRIs may impair cognitive performance to an extent, and indeed Bari et al. (2010) demonstrated that low SSRI doses impaired, while larger doses improved, behavioural flexibility in the rat, although an analogous

human experiment has yet to be performed. An explanation for this is that low doses of SSRIs increase serotonin levels to the point where all serotonergic autoreceptors are ‘filled’, leading to an inhibition of serotonin discharge (Blier, Serrano, & Scatton, 1990). Higher doses hypothetically bypass this inhibitory mechanism, allowing for a net increase in prefrontal serotonin availability (Bymaster et al., 2002; Koch et al., 2002). This has been demonstrated empirically, wherein lower doses of SSRIs reduced serotonin concentration in the primate brain while higher doses increased serotonin concentraion (Nord, Finnema, Halldin, & Farde, 2013).

Alongside dosage, cognitive findings in the medicated patient group could be linked to duration of medication treatment, as a study has found that in the early stages of SSRI treatment, patients with OCD showed declines in cognitive and memory abilities compared to before they started treatment (Sayyah, Eslami, AlaiShehni, & Kouti, 2016). Patients on higher doses of SSRIs in my studies may have been receiving treatment for longer (as early stages of treatment often involve administration of smaller doses at first) and thus did not experience cognitive dysfunction associated with early stages of treatment. Unfortunately, I did not obtain information about treatment duration from my adolescent patients and hence am unable to explore this theory.

All things considered, it is inappropriate to conclude that low dose SSRIs were definitely driving abnormal behaviour in medicated patients as dosage did not correlate with task measures that were significantly different in medicated compared to control participants.

Random and erratic responding displayed by the medicated group is also expressed in healthy children with ADHD traits (Dubois et al., 2020), suggesting that the medicated patients are perhaps more impulsive than unmedicated and control groups. Nonetheless, there is no evidence to suggest that SSRIs increase impulsive tendencies in people, and moreover in some populations they appear to actually reduce impulsivity (Butler et al., 2010).

In contrast to the majority of research reporting that SSRIs enhance cognition, Gruner et al. (2012) found that children with OCD medicated with SSRIs displayed worse performance on the WCST while medication-naïve patients showed no impairment. More recently, Apergis-Schoute et al. (in-prep) reported that SSRI-medicated patients performed worse compared to unmedicated patients during acquisition learning on a probabilistic reversal learning task. As mentioned in previous chapters, the medicated group in this thesis may have had a more severe form of the disorder to have necessitated being treated with psychotropic medication, even if medicated and unmedicated participants with OCD were equivalent in terms of symptom severity measured via clinical scales such as the CY-BOCS. This is because the medication may have been successful in reducing clinician

rated symptoms associated with the disorder, but disorder-related abnormalities in decision-making are perhaps more resistant to treatment. Relevant to this explanation, it may be that lower doses of SSRIs are not effective in improving cognition in this population compared to higher doses of SSRIs, which could account for the correlations found between SSRI dosage and IQ/decision-making reported in the chapters of this thesis.

Nonetheless, further research is needed to truly understand the exact neural and behavioural mechanisms affected by SSRIs in OCD.

7.5 Effects of Age, IQ, and Working Memory

Aside from illuminating the effects of OCD and medication on learning and decision-making, the studies conducted in this thesis have revealed significant influences of age, IQ, and working memory on task performance. First, regardless of OCD status, older participants outperformed younger participants across several tasks' measures, and even displayed more exploitation and better choice value sensitivity (lower drift rates) on the sequential decision-making task in Chapter 4. This is consistent with research showing that random exploratory decision-making diminishes in favour of maximisation strategies as children and adolescents become older (Plate, Fulvio, Shutts, Green, & Pollak, 2018; Somerville et al., 2017). My findings demonstrate that important constructs of learning and decision-making are age-dependent, and that adolescents with OCD are still expressing maturation of these functions, albeit at a potentially reduced rate compared to healthy adolescents, as task performance remains atypical in this group even when controlling for age.

Next, IQ and working memory correlated with several performance measures including model-based control, exploitation, and choice value sensitivity in Chapter 4 regardless of OCD status, suggesting that higher order cognitive abilities are potential protective factors against atypical decision-making in adolescent-OCD. This has implications for future work exploring cognitive training as a potential treatment for adolescents and children with OCD. However, evidence for the benefits of cognitive training, particularly working memory training, is contentious. On the one hand, working memory training has been found to elevate symptoms of anxiety and depression in adolescents (Beloe & Derakshan, 2020) and the use of computerised cognitive games has been found to improve processing speed, working memory, executive functioning, and verbal memory in older adults (Bonnechère, Langley, & Sahakian, 2020). In contrast, a meta-analysis synthesising findings from 23 studies reported that benefits of working memory training were short-term and did not generalise to other cognitive constructs (Melby-Lervåg & Hulme, 2013). Very few studies have explored cognitive training in the context of OCD. One of these few studies reported that visuospatial

memory training improved memory abilities and reduced symptom severity in adults with OCD (Park et al., 2006) but another study found that patients with OCD showed improvements over time regardless of whether they were allocated to visuospatial memory training or waitlisted (Buhlmann et al., 2006). Other studies also report that teaching children and adults with OCD learning and memory strategies fails to improve their performance on certain tasks (Batistuzzo et al., 2015; Chamberlain, Blackwell, Fineberg, Robbins, & Sahakian, 2006). Thus, evidence supporting therapeutic and functional benefits of cognitive training in OCD is limited, and there is in actuality more documentation of conventional treatments such as cognitive behavioural therapy and serotonergic medication (although findings in this thesis may suggest otherwise) improving cognitive abilities and symptoms in children with OCD (Andrés et al., 2008; Huyser et al., 2010). In fact, the best way to prevent cognitive decline in OCD is likely via early detection and long-term conventional treatment, as research shows that rates of remission following medication treatment are highest in younger patients with OCD (Mancebo et al., 2008).

7.6 Implications for Education

Adolescents and children with OCD are significantly disadvantaged in educational settings (Negreiros et al., 2018; Piacentini et al., 2003) and as a result affected youths are less likely to complete secondary school and/or university (Pérez-Vigil et al., 2018). Conversely, findings from this thesis suggest that deficits in flexibility and goal-directed control (thought to be cognitive hallmarks of adult OCD) are not prominent in adolescents with OCD. Instead, adolescents with OCD express atypical decision-making specifically in the form of maladaptive exploration.

Being able to flexibly update between exploration and exploitation appropriately is an integral part of learning (Addicott et al., 2017). Particularly, in childhood, exploration and novelty-seeking are healthy behaviours that enable learning new skills and information about the world, and are thus crucial for development (Gopnik, 2020; Kidd & Hayden, 2015). Although exploration is deemed to be healthy behaviour in children, adolescents with OCD seem to be especially impaired at disengaging from exploration leading to poor performance on tasks such as the probabilistic reversal learning task in Chapter 6. This inability to appropriately balance exploration with exploitation may be impacting their ability to learn information and master new skills, particularly in situations rife with uncertainty. School and university may present unique and unexpected challenges in the form of substantial workload and social pressure, of which youths with OCD may be unable to cope with as a result of their insufficient learning and decision-making abilities. This has implications for educational centres devoting time and resources providing support to youths with OCD. Extensive

meetings with school counsellors to discuss potential stressors or uncertain elements of school/university may benefit affected students. In addition, extra time to complete assignments or examinations may help to reduce stress and improve performance in students with OCD. Such support should be directed in particular towards younger students and students with a history of low performance on intelligence tests, as I have found that adolescents with OCD who are younger and have lower IQ are more susceptible to cognitive impairment.

Nonetheless, it is unknown whether atypical decision-making/exploration on reinforcement learning tasks truly corresponds to reduced education attainment in youths with OCD. It may be that abnormal exploration is a consequence of other disrupted functions such as inefficient evidence accumulation and overreliance on sensory modalities, in line with the earlier discussed model of OCD proposed by Fradkin, Adams et al. (2020). It is also possible that other domains found to be impaired in OCD such as strategy implementation and goal-directed planning (Batistuzzo et al., 2015; Negreiros et al., 2019) are driving poor performance in school. Alternatively, patients' hyper-focus on the contents of their obsessions may be affecting their concentration on school work. To derive solid conclusions, future research first needs to establish 1) why adolescents with OCD show abnormally active exploration, and 2) whether abnormal exploration directly impacts school performance.

7.7 Limitations and future directions

As a result of national lockdown restrictions introduced to curb the spread of Covid-19, data collection was halted for several months and I was unable to collect data from as large a sample size as initially projected. Nonetheless, I have now resumed data collection for the purposes of publishing my findings and hope to achieve a sample size large enough for each task to enable more concrete and reliable inferences to be drawn.

Next, the experiments in this thesis were effective in highlighting maladaptive exploration during probabilistic decision-making in adolescent OCD, but paradigms used were unfortunately not optimised for understanding exact reasons contributing to over-exploration. I discussed various possible factors in an earlier section that could promote a bias for exploration in adolescents and adults with OCD, but these factors can only be confirmed in future work employing well-designed paradigms and more sophisticated computational models (e.g. a task and model that can dissociate information-seeking exploration from random exploration).

Future work should also attempt to ascertain the neurological basis for exploratory decision-making in OCD, as for now we are only able to make assumptions based on existing neuroimaging research

that have employed cognitive tasks unrelated to explore-exploit processes. In addition, it would be instrumental to understand how exploratory decision-making is linked to heightened ERN and conflict monitoring, which are robust neurocognitive markers of early- and late-onset OCD.

Although the work presented in this thesis contributes significantly to the admittedly sparse body of literature investigating cognition in child- and juvenile-OCD, it is difficult to draw inferences from my findings about how adolescents with OCD compare to adults with OCD. This is due to the studies in this thesis comparing adolescent patients to healthy adolescent patients who are still in the process of developing executive functions. Hence, upcoming research should directly compare decision-making displayed by adults with OCD to that of adolescents with OCD while simultaneously taking into account possible effects of disorder duration and age of disorder onset. Longitudinal methods would be even more useful in determining how decision-making becomes atypical with age in OCD, and would also enable inferences related to causality, i.e. does OCD promote abnormal exploration or does a tendency for exploration drive compulsions? Large-scale cohort studies, such as the recently launched Adolescent Brain Cognitive Development study (Casey et al., 2018) based in the United States, have just begun to delve into how neurocognitive mechanisms interact with and promote symptoms of psychiatric disorders over time in children and adolescents. Findings from these ongoing longitudinal studies will be integral to unravelling the complex cognitive structure of OCD that appears to shapeshift across the lifespan.

7.7.1 Accounting for cognitive and clinical heterogeneity: a personalised approach to diagnosis and treatment?

It is noteworthy that variance in performance across all tasks was high within the OCD group, which led to the use of non-parametric statistical analysis in all experimental chapters. This variance in decision-making performance may reflect the highly heterogeneous nature of the disorder, wherein symptom profiles differ strikingly from patient to patient (Bloch et al., 2008). This suggests issues with ‘one-size-fits-all’ diagnosis and treatment recommendations, and research thus far has attempted to assess treatment effectiveness based on symptom profiles. For instance, children with contamination symptoms of OCD reportedly display better responsiveness to CBT (Ginsburg, Kingery, Drake, & Grados, 2008), although a later study found that children with symmetry/hoarding symptoms show better responding to CBT (Højgaard et al., 2018).

Rather than accounting for only symptom profiles when assigning clinical labels and recommending treatment, it may be necessary to consider the cognitive characteristics of individual patients. One study so far has studied the relationship between cognition and treatment effectiveness

in paediatric OCD patients, and found that patients with poor performance on executive function tasks showed better responsiveness to CBT compared to patients with superior executive functioning (Hybel, Mortenson, Lambek, Højgaard, & Thomsen, 2017). Moreover, specific cognitive traits are found to be associated with certain symptom dimensions in adult OCD (i.e contamination symptoms were associated with better memory, checking symptoms were associated with poor inhibition, and symmetry/hoarding symptoms were associated with poor memory and inhibition) (Hashimoto et al., 2008), although evidence for this is unclear in paediatric OCD samples (Hybel, Mortenson, Højgaard, Lambek, & Thomsen, 2017).

In future work, it would be valuable to assess whether the neurocognitive features reported in this thesis can aid in clinical diagnosis and tailored treatment for adolescents with OCD. For instance, youths with OCD who are more exploratory on a task may have a different form of OCD and different support needs from patients who display more perseverative behaviour. Findings from the tasks reported in this thesis are a promising starting point for investigating this notion. At present, the tasks were analysed independently from each other, but it would be instrumental to integrate findings across all experimental chapters to derive a holistic picture of learning and decision-making in adolescent OCD and understand how distinct cognitive profiles relate to different symptoms and severity levels. One concrete way to achieve this is by applying computational methods such as a partial least squares (PLS) regression (Helland, 1990). This method in particular is used to identify a set of independent components from various predictors (i.e linear combinations of task performance scores and parameter values) that show the strongest association with response variables of interest (i.e. symptom severity or symptom profiles). In future manuscripts, I plan to use this method to investigate how a combination of behavioural signatures across different tasks are associated with OCD severity, medication usage/dosage, and symptom profiles. This individualized approach to cognitive and clinical phenotyping, moving away from traditional clinical labels, may transform and improve the field of psychiatry as we know it currently.

Conclusions

The work presented in this thesis contributes to the recent growing body of research investigating cognition and development in OCD. Establishing the neuropsychological profile of child/juvenile-OCD has been difficult thus far, as paediatric patients appear generally unimpaired on several cognitive domains, even those considered potential endophenotypes of adult-OCD.

By employing a combination of well-validated and novel paradigms, I have demonstrated that atypical decision-making in adolescent OCD is most pronounced on tasks with stochastic choice outcomes compared to tasks with stable or deterministic pay-offs. These findings strongly imply that young people with OCD are affected by environmental volatility, consistent with reports of intolerance of uncertainty in this clinical population.

Computational methods used in this thesis have been instrumental in unravelling the dynamics of decision-making portrayed by patients, which would have been otherwise too subtle to be detected using standard frequentist analyses. In particular, fitting reinforcement learning models to data has revealed that adolescents with OCD show a bias for exploratory over exploitative decision-making. This indicates that young patients are making decisions inconsistent with how rewarding or valuable different possible choices are. Additionally, when compared to healthy adolescents, their choices and meta-cognition are less influenced by prediction errors, implying dampened feedback processing in this population. These behaviours are potentially analogous to real-life compulsions that persist despite being inconsistent with information present in the environment (e.g. continuously checking that a stove is off even though evidence overwhelmingly suggests that it is) and yielding no concrete benefits. Ultimately, my findings signify the importance of utilising computational methods to improve understanding of complex behavioural processes such as decision-making.

Experiments in this thesis have also revealed that adolescents with OCD show comparable cognitive flexibility, model-based behaviour, and action-confidence coupling to healthy adolescents. These findings are intriguing as deficits in these domains are thought to be intertwined with adult OCD symptomatology. Distinctions may be attributed to 1) certain cognitive functions only emerging in adulthood or as disorder duration prolongs, 2) being a consequence of developmental artefacts, wherein group differences are undetected due to healthy adolescents displaying age-related underperformance on several tasks, or 3) adolescent-OCD being a subtype of, or even a separate psychiatric disorder from, adult-OCD. Nonetheless, exploratory decision-making has been detected in both adolescent and adult OCD populations, indicating that it is a stable trait of the disorder. Future

research should focus on understanding factors influencing frequent exploration in OCD, how it relates to clinical symptoms, and neurobiological mechanisms underlying such behaviour.

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